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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA (SAN FRANCISCO)

LINDA GOSHERT, individually and on behalf of
all others similarly situated,

Plaintiff,

v.

COMPANA PET BRANDS,

Defendant

No.: 3:22-cv-04617-JSC

**NOTICE OF MOTION AND MOTION TO
DISMISS; MEMORANDUM OF POINTS
AND AUTHORITIES**

Date: November 3, 2022

Time: 9:00 AM

Dept: San Francisco, Courtroom 8, 19th Floor

Judge: Hon. Jacqueline S. Corley

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1 **NOTICE OF MOTION AND MOTION TO DISMISS**

2 PLEASE TAKE NOTICE that on Thursday, November 3, 2022 at 9:00 AM or as soon as
3 counsel may be heard, before the Honorable Jacqueline Scott Corley, San Francisco Courthouse, 450
4 Golden Gate Avenue, San Francisco, California, Courtroom 8, 19th Floor, Defendant Compana Pet
5 Brands will, and do, move under Federal Rule of Civil Procedure 12(b)(6) and 12(b)(1) to dismiss
6 Plaintiff Linda Goshert’s Class Action Complaint (Doc. 1). This motion is based on this Notice of Mo-
7 tion and Motion, the Memorandum of Points and Authorities, the arguments of counsel, and such other
8 submissions and material that the Court may consider.

9 **STATEMENT OF ISSUES TO BE DECIDED**

10 1. Whether Plaintiff’s Complaint fails to state a claim upon which relief can be granted
11 under Federal Rule of Civil Procedure 12(b)(6) and whether Plaintiff lacks standing to seek injunctive
12 relief or represent purchasers of unpurchased products under Federal Rule of Civil Procedure 12(b)(1).

13 2. Whether Plaintiff’s Complaint satisfies the pleading standard under Federal Rule of
14 Civil Procedure 8(a) and the heightened pleading standard under Federal Rule of Civil Procedure 9(b)
15 for any of her legal claims or factual allegations.

16 **MEMORANDUM OF POINTS AND AUTHORITIES**

17 **INTRODUCTION**

18 Plaintiff Linda Goshert thought that Doggie Dailies Hip & Joint Supplement for Dogs (“Soft
19 Chews”), containing the ingredients glucosamine and chondroitin, “would effectively treat her dog’s
20 hip and joint pain and would support connective tissue and joint movement.” But now she alleges that
21 “[d]ecades of studies”—or at least the four selectively quoted sources dated between 2003 and 2017—
22 debunk the notion that supplements containing glucosamine and chondroitin effectively promote joint
23 health. Those sources may be relevant to some case, but they are not relevant to this one. That is be-
24 cause the “studies” that purportedly disprove representations about the Soft Chews deal only with dis-
25 ease treatment, not supporting or promoting joint health. And even if they were somehow relevant,
26 these studies would contradict, not support, Goshert’s allegations. Worse yet, Goshert does not even
27 allege that the product did not work on her dog.

28 All of Goshert’s claims against Defendant Compana Pet Brands are based on this disconnect.

1 She thus fails to allege that the labels are false or misleading with the plausibility required under Rule
2 8 and the particularity required under Rule 9(b). Each of her claims also has other problems on top of
3 this fundamental one. The result should be a dismissal of the Complaint under Rule 12(b)(6) or under
4 Rule 12(b)(1).

5 BACKGROUND

6 ***The Statements.*** Goshert alleges that in March 2022, she bought a bottle of Doggie Dailies Hip
7 & Joint Supplement for Dogs from Amazon.com. Compl. ¶ 16. Goshert alleges that she purchased this
8 product “numerous times over the years.” *Id.* The Soft Chews’ label states that the product “Promotes
9 Healthy Joints, Comfort, and Mobility.” *Id.* ¶ 3. Goshert also alleges that Compana “made [these] ad-
10 ditional representations” on Amazon’s website: (1) “Doggie Dailies is a safe and effective hip and
11 joint soft chew your dog will love. Our glucosamine dog treats are specially formulated to help pro-
12 mote healthy joints, mobility, and flexibility. A daily dose of Doggie Dailies soft chews can help sup-
13 port your dog’s mobility and overall joint health.”; (2) “Promotes Cartilage Development”; and (3)
14 “Specifically Formulated to Support Joint Function” (the three Amazon representations and the label
15 statement are collectively, the “Statements”). *Id.* ¶ 16. Goshert “understood these statements to mean”
16 that the Soft Chews “would effectively treat her dog’s hip and joint pain and would support connective
17 tissue and joint movement,” and gave the Soft Chews to her dog as directed. *Id.*

18 Although Goshert alleges that the Soft Chews are “ineffective,” “worthless,” “a sham,” *id.*
19 ¶¶ 9, 12, 88, Goshert never alleges that the Supplements had no effect on her dog, *see id.* ¶ 16. Yet
20 Goshert still alleges that the Statements are false and misleading, as shown by “[d]ecades of studies
21 and peer-reviewed tests.” *Id.* ¶ 9. In support, Goshert cites only four authorities: Plumb’s Veterinary
22 Handbook (“Plumb’s”), the Banfield Journal, the Moreau study, and the Scott study.¹ *See id.*

24 ¹ The Plumb’s handbook is attached as Attachment A to the September 13, 2022 Declaration of Jen-
25 nifer Lee, attached as Exhibit 1. The Banfield Journal article is attached as Attachment B. The Moreau
26 study is attached as Attachment C. The Scott study is attached as Attachment D. *See Ex. 1 Atts. A–D.*
27 the Court does not consider material beyond the pleadings on a motion to dismiss, “[e]xceptions to this
28 rule include material submitted as part of the complaint or relied upon in the complaint, and material
subject to judicial notice.” *Secure Cam, LLC v. Tend Insights, Inc.*, 351 F. Supp. 3d 1249, 1253 (N.D.
Cal. 2018) (quoting *Lee v. City of Los Angeles*, 250 F.3d 668, 688–89 (9th Cir. 2001)); *see also Davis*
v. HSBC Bank Nevada, N.A., 691 F.3d 1152, 1160 (9th Cir. 2012) (“Under the incorporation by refer-
ence doctrine in this Circuit, . . . courts may take into account documents whose contents are alleged in

¶¶ 10-11, 13.

Sources Cited in Complaint. At best, these sources are irrelevant. In the first place, none of them address (and Goshert does not allege that they address) the efficacy of the Soft Chews, or any Doggie Dailies product. *See generally* Ex. 1 Atts. A–D. Nor does Goshert allege that any of these sources address a product that contains glucosamine and chondroitin with the Soft Chews’ concentration, combination, amount per dose, or directed dosage. And even more to the point, each authority addresses whether glucosamine and chondroitin, as ingredients in other canine nutraceuticals, treat joint disease or osteoarthritis. Plumb’s addresses whether glucosamine and chondroitin can be “used as an adjunctive treatment for osteoarthritis or other painful conditions.” *Id.* Att. A at 429. The Banfield Journal analyzes whether glucosamine and chondroitin in combination effectively treat joint disease. *See id.* Att. B at 3. The Moreau study sought to find “the best treatment for dogs with [the diagnosed condition of] osteoarthritis.” *Id.* Att. C at 323. And the Scott study aimed to “assess the safety and efficacy of [glucosamine and chondroitin] for the treatment of clinical osteoarthritis (OA) in dogs.” *Id.* Att. D at 318.

Further, while irrelevant to efficacy for promoting healthy joints, two of Goshert’s four authorities acknowledge that glucosamine and chondroitin may be effective for treating joint disease. Plumb’s states that while “efficacy is uncertain,” glucosamine/chondroitin nutraceuticals “can be used as an adjunctive treatment for osteoarthritis or other painful conditions.” *Id.* Att. A at 429. Plumb’s also reports that “[t]hese compounds may be useful in treating osteoarthritis or other painful conditions in domestic animals, [even though] large, well-designed controlled clinical studies proving efficacy were not located.” *Id.* “The Banfield Journal agrees that although “strong clinical evidence of efficacy is lacking, and these compounds are understudied,” evidence exists “that a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals improves symptoms associated with joint disease in dogs and cats.” *Id.* Att. B at 3.

Goshert’s Complaint. On August 10, 2022, Goshert sued Compana on behalf of herself and a

a complaint and whose authenticity no party questions, but which are not physically attached to the [plaintiff’s] pleading.”) (cleaned up). The Court may properly consider these sources because Goshert incorporates them by reference.

putative class defined as “[a]ll persons in the State of California who purchased the Supplements.” Compl. ¶ 23. Goshert defines “Supplements” as both the Soft Chews she purchased and three other Doggie Dailies products that she did not purchase: (1) Senior Essentials Advanced Hip & Joint Supplement for Senior Dogs; (2) 5-in-1 Multivitamin Soft Chews for Dogs; and (3) Advanced 10-in-1 Senior Multivitamin. *Id.* ¶ 1.

The Complaint asserts seven counts. **Counts I, II, and III** assert violations of the Consumer Legal Remedies Act (“CLRA”), Cal. Civ. Code § 1750, *et seq.*; California’s False Advertising Law (“FAL”), Cal. Bus. & Prof. Code § 17500, *et seq.*; and California’s Unfair Competition Law (“UCL”), Cal. Bus. & Prof. Code § 17200, *et seq.*; **Counts IV and V** assert breach of express warranty, and breach of implied warranty under the Song-Beverly Consumer Warranty Act, Cal. Civ. Code § 1792, *et seq.*, and California Commercial Code § 2314; **Count VI** alleges fraud; and **Count VII** alleges unjust enrichment. All Counts should be dismissed.

STANDARD OF REVIEW

“[A] complaint must contain sufficient factual matter, accepted as true, to state a claim to relief that is plausible on its face.” *Miller v. Sawant*, 18 F.4th 328, 336 (9th Cir. 2021) (quoting *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009)) (cleaned up). “A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged.” *Id.* “A pleading that offers labels and conclusions or a formulaic recitation of the elements of a cause of action will not do. Nor does a complaint suffice if it tenders naked assertions devoid of further factual enhancement.” *Nayab v. Cap. One Bank (USA), N.A.*, 942 F.3d 480, 500 (9th Cir. 2019) (quoting *Ashcroft*, 556 U.S. at 678) (cleaned up). In other words, [w]here the well-pleaded facts do not permit the court to infer more than the mere possibility of misconduct, the complaint has alleged—but it has not shown—that the pleader is entitled to relief.” *William O. Gilley Enterprises, Inc. v. Atl. Richfield Co.*, 588 F.3d 659, 668 (9th Cir. 2009) (cleaned up).

ARGUMENT

I. Goshert fails to state a claim under the CLRA, FAL, and UCL (Counts I–III).

A. Goshert fails to plausibly allege that the Statements are false or misleading.

Goshert’s claims under the CLRA, FAL, and the UCL’s fraudulent and unfair prongs fail be-

1 cause Goshert fails to plausibly allege that reasonable consumers could be misled by the Statements.
2 Compl. ¶¶ 29–51, 58–63; *see Hadley v. Kellogg Sales Co.*, 273 F. Supp. 3d 1052, 1063 (N.D. Cal.
3 2017) (analyzing these three statutes together and collecting cases); *Maxwell v. Unilever U.S., Inc.*,
4 2018 WL 1536761, at *5 (N.D. Cal. Mar. 29, 2018). Whether a business practice is deceptive or mis-
5 leading under these California statutes is governed by the “reasonable consumer test,” under which a
6 plaintiff “must show that members of the public are likely to be deceived.” *Williams v. Gerber Prod-*
7 *ucts Co.*, 552 F.3d 934, 938 (9th Cir. 2008) (cleaned up). This “requires more than a mere possibility
8 that [a] label might conceivably be misunderstood by some few consumers viewing it in an unreasona-
9 ble manner.” *Ebner v. Fresh, Inc.*, 838 F.3d 958, 965 (9th Cir. 2016) (cleaned up). It “requires a proba-
10 bility that a significant portion of the general consuming public or of targeted consumers, acting rea-
11 sonably in the circumstances, could be misled.” *Id.* (cleaned up).

12 “When UCL, CLRA, and FAL claims are premised on misleading advertising or labeling, Rule
13 9(b) requires the plaintiff to allege the particular circumstances surrounding [the] representations’ at
14 issue.” *In re Arris Cable Modem Consumer Litig.*, 2018 WL 288085, at *8 (N.D. Cal. Jan. 4, 2018)
15 (citing *Kearns v. Ford Motor Co.*, 567 F.3d 1120, 1126 (9th Cir. 2009) (explaining that when a plaintiff
16 “allege[s] a unified course of fraudulent conduct and rel[ies] entirely on that course of conduct as the
17 basis of that claim . . . the claim is said to be ‘grounded in fraud’ or to ‘sound in fraud,’ and the plead-
18 ing . . . as a whole must satisfy the particularity requirement of Rule 9(b)”). “To properly plead fraud
19 with particularity under Rule 9(b), a pleading must identify the who, what, when, where, and how of
20 the misconduct charged, as well as what is false or misleading about the purportedly fraudulent state-
21 ment, and why it is false.” *Davidson v. Kimberly-Clark Corp.*, 889 F.3d 956, 964 (9th Cir. 2018) (hold-
22 ing that claims for false or misleading advertising under the CLRA, FAL, and UCL are “grounded in
23 fraud” and applying Rule 9(b)) (cleaned up). Goshert is thus “required not simply to adequately plead
24 that reasonable consumers are likely to be deceived” by the Statements “but also why the [Statements
25 are] false.” *Id.* at 965 n.2.

26 “Several courts . . . have observed that a study concluding that a product does not alleviate os-
27 teoarthritis symptoms does not speak to whether that the same product supports general joint health.”
28 *Lytle v. Nutramax Lab’ys, Inc.*, 2019 WL 8060070, at *5 (C.D. Cal. Sept. 26, 2019) (collecting cases);

1 *see, e.g., Eckler v. Wal-Mart Stores, Inc.*, 2012 WL 5382218, at *7 (S.D. Cal. Nov. 1, 2012) (“The
2 studies allegedly show that glucosamine doesn’t alleviate the symptoms of osteoarthritis in the hip and
3 knee. That is a very particular showing with respect to a degenerative joint disease and . . . it doesn’t
4 address the far more general claim . . . that glucosamine is good for the body’s joints.”); *McCrary v.*
5 *Elations Co.*, 2013 WL 6402217, at *3 (C.D. Cal. April 24, 2013) (“[T]he studies pertaining to the in-
6 effectiveness of [these] ingredients in the treatment of osteoarthritis are inapposite. These studies do
7 not plausibly demonstrate that [the product] does not improve joint comfort, flexibility, or health.”);
8 and *Padilla v. Costco Wholesale Corp.*, 2013 WL 195769, at *3 (N.D. Ill. Jan. 16, 2013) (“[T]he . . .
9 product label does not claim to be effective for the treatment of osteoarthritis. Thus, clinical studies
10 regarding the ineffectiveness of glucosamine or chondroitin in the treatment of osteoarthritis does not
11 have any bearing on the truthfulness of the actual representations made on the . . . product label.”).
12 These cases “reflect the principle that a study’s conclusion must **directly** address the misrepresentation
13 it is cited to debunk.” *Lytle*, 2019 WL 8060070, at *5 (emphasis added).

14 Goshert fails to plausibly allege “what is false or misleading about the purportedly fraudulent
15 statement[s], and why it is false” because her four scientific authorities do not directly address the Soft
16 Chews’ Statements. *See* Compl. ¶¶ 10–11, 13. Rather, they address the efficacy of some formulation
17 of glucosamine and chondroitin in *treating* joint disease or osteoarthritis. *See supra* at 2–3. But the
18 Statements do not claim that the Soft Chews treat joint disease or osteoarthritis; they speak only in ge-
19 neric terms about promoting or supporting joint health: (1) “Promotes Healthy Joints, Comfort, and
20 Mobility”; (2) “Doggie Dailies is a safe and effective hip and joint soft chew your dog will love. Our
21 glucosamine dog treats are specially formulated to help promote healthy joints, mobility, and flexibil-
22 ity. A daily dose of Doggie Dailies soft chews can help support your dog’s mobility and overall joint
23 health.”; (3) “Promotes Cartilage Development”; and (4) “Specifically Formulated to Support Joint
24 Function.”² Compl. ¶ 16; *see generally Levitt v. Yelp! Inc.*, 765 F.3d 1123, 1135 (9th Cir. 2014)

25
26 ² Goshert alleges that Compana made other representations about the Soft Chews on Doggie Dailies’
27 website, but she never alleges that she relied on these statements before purchasing the Soft Chews.
28 *See* Compl. ¶¶ 3, 12. These statements cannot support Goshert’s CLRA, UCL, and FAL claims, which
require reliance. *See, e.g., Lanovaz v. Twinings N. Am., Inc.*, 2014 WL 46822, at *6 (N.D. Cal. Jan. 6,
2014); *In re Ferrero Litig.*, 794 F. Supp. 2d 1107, 1111–12 (S.D. Cal. 2011).

1 (“[E]valuating a complaint’s plausibility is a context-specific endeavor that requires courts to draw on
2 judicial experience and common sense.”) (cleaned up).

3 Yet even if they were somehow relevant, these studies would contradict, not bolster, Goshert’s
4 allegations that the Soft Chews do not support joint health.³ See Ex. 1 Att. D (Scott) at 318–19, 321
5 (compiling study results and noting that clinical trials in dogs revealed “variable clinical efficacy”;
6 “[T]here is evidence that various glucosamine/chondroitin products are bioavailable in the dog and
7 provide a treatment benefit in induced canine models of osteoarthritis.”); *id.* Att. C (Moreau) at 323
8 (“A mixture of [glucosamine and chondroitin] has previously been shown to provide prophylactic pro-
9 tection against synovitis [(i.e., swollen joints)] to retard the degenerative process synergistically and to
10 modulate the metabolism of articular cartilage.”); *id.* Att. A (Plumb’s) at 429 (“Glucosamine also
11 regulates synthesis of collagen and proteoglycans in cartilage and has mild antiinflammatory effects
12 due to its ability to scavenge free radicals Chondroitin sulfate possesses several pharmacologic
13 effects. It appears to inhibit destructive enzymes in joint fluid and cartilage In joint cartilage, it
14 stimulates the production of glycosaminoglycans and proteoglycans.”); *id.* Att. B at 4 (Banfield)
15 (“Most efficacy studies involving the combination of the two compounds are conducted with hu-
16 mans—extrapolating from these studies, it is recommended to use these nutraceuticals for Pets with
17 mild to moderate joint disease.”). Consulting the sources shows that Goshert has “obviously cherry-
18 picked all of the most negative language from the [studies] that could potentially support her claims
19 and has ignored” everything else. *Route v. Mead Johnson Nutrition Co.*, 2013 WL 658251, at *5 (C.D.
20 Cal. Feb. 21, 2013).

21 Goshert’s claims are all but identical to recently rejected claims involving another canine joint
22 health supplement sold by Compana. In *Perry v. Manna Pro Products, LLC*,⁴ the plaintiff alleged that
23 the statement, “Helps support[] joint health, flexibility and cartilage in dogs of all ages, including old-
24 er, previous injured working dogs,” on a different brand’s hip and joint supplements was false and
25

26 ³ The Court “need not accept as true allegations that contradict matters properly subject to judicial no-
27 tice or by exhibit.” *Gonzalez v. Planned Parenthood of Los Angeles*, 759 F.3d 1112, 1115 (9th Cir.
28 2014); see, e.g., (“*Love v. Handlery Hotels, Inc.*, 2021 WL 2531090, at *5 (N.D. Cal. June 21, 2021)
29 (“Love asserts that the website left him ‘essentially ignorant’ about the Hotel’s accessibility . . . but
30 this is contradicted by the website he incorporated by reference into the complaint.”).

⁴ In March 2022, Manna Pro Products, LLC rebranded as Compana Pet Products.

misleading under New York law based on the same four scientific sources that Goshert cites here. 2022 WL 3585611, at *1–*2 (E.D. Mo. Aug. 22, 2022). After reviewing the sources, the court held that “they are focused on the effectiveness of glucosamine or chondroitin in the treatment of osteoarthritis, joint disease, and joint pain—topics which are not mentioned [on] Defendant’s product labels or website.” *Id.*, at *4. In so holding, the court rejected the plaintiff’s argument that the sources’ “focus on osteoarthritis” is a “‘distinction without a difference’ because it is well known that joint health (or lack thereof) is a symptom of osteoarthritis.” *Id.*, at *3; *see* Compl. ¶ 12 (alleging that the Supplements claim to treat osteoarthritis symptoms). In the end, the court dismissed with prejudice, concluding that the plaintiff failed to plausibly allege a false or misleading representation: “[I]t is Plaintiff’s burden to plausibly plead falsity or deception. Her only attempt to do so here is to cite to the above-noted publications and to state that the Supplements had no impact on her dog’s osteoarthritis or joint pain. But the alleged representations on which Plaintiff relied do not claim otherwise.” *Id.*, at *5. So too here.

Finally, Goshert fails to allege with particularity—or at all for that matter—how the Soft Chews did not work on her dog. Goshert alleges that she “gave her dog the Doggie Dailies Soft Chews as directed.” Compl. ¶ 16. That’s it. Nowhere does Goshert allege that the Soft Chews did not “treat her dog’s hip and joint pain” or did not “support [her dog’s] connective tissue and joint movement.”⁵ *Id.*; *see Perry*, 2022 WL 3585611, at *5 (rejecting plaintiff’s conclusory allegation that “the Supplements had no impact on her dog’s osteoarthritis or joint pain”); *Eckler*, 2012 WL 5382218, at *3 n.2, *8 (finding plaintiff’s conclusory allegation that the glucosamine product at issue “did not rebuild her cartilage, lubricate her joints or improve her joint comfort as represented” speculative and noting that, as much as plaintiff’s claim turned on her own experience, she needed to “say far more than, in essence, ‘I took Equate and didn’t feel any better’”); *accord, e.g., Castillo v. Unilever U.S., Inc.*, 2022 WL 704809, at *5 (N.D. Ill. 2022) (dismissing plaintiffs’ fraud-based claims when they “failed to allege that the products they purchased failed to work as advertised for *them*”) (emphasis in original).

⁵ And if Goshert tried to amend by simply asserting these allegations, it would create new plausibility problems. Goshert cannot plausibly allege that she somehow measured her dog’s “hip and joint pain” or the Soft Chews efficacy at “support[ing her dog’s] connective tissue and joint movement” before and after the Soft Chews’ use. Compl. ¶ 16; *see, e.g., Eckler*, 2012 WL 5382218, at *3 n.2; *see generally Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007) (“Factual allegations must be enough to raise a right to relief above the speculative level[.]”).

1 **B. Goshert’s alleged violations of the CLRA, FAL, and UCL claims are unactionable**
2 **lack of substantiation claims.**

3 Rather than support the Statements’ falsity, Goshert’s sources expose Goshert’s theory as an
4 unactionable “lack of substantiation” claim. “It is well settled that private litigants may not bring false
5 advertising claims based on an alleged lack of substantiation.” *Yamasaki v. Zicam LLC*, 2021 WL
6 4951435, at *4 (N.D. Cal. Oct. 25, 2021) (citing *Nat’l Council Against Health Fraud Inc. v. King Bio*
7 *Pharms. Inc.*, 107 Cal. App. 4th 1336, 1345, 133 Cal. Rptr. 2d 207 (2003)). “[A]n advertising claim is
8 false if it has actually been disproved, that is if the plaintiff can point to evidence that directly conflicts
9 with the claim.” *Kwan v. SanMedica Int’l, LLC*, 2015 WL 848868, at *4 (N.D. Cal. Feb. 25, 2015)
10 (cleaned up); *see also Tubbs v. AdvoCare Int’l, L.P.*, 785 F. App’x 396 (9th Cir. 2019) (“The falsity of
11 the advertising claims may be established by testing, scientific literature, or anecdotal evidence.”
12 (quoting *King Bio*, 107 Cal. App. 4th at 1348)). For this reason, “a plaintiff’s reliance on a lack of sci-
13 entific evidence or inconclusive, rather than contradictory, evidence is not sufficient to state a claim.”
14 *Bronson v. Johnson & Johnson, Inc.*, 2013 WL 1629191, at *8 (N.D. Cal. Apr. 16, 2013).

15 Though Goshert alleges that the products are a “worthless” “a sham,” Compl. ¶¶ 9, 88, the sci-
16 entific literature relied on to prove falsity are, at best, irrelevant to these allegations and, at worst, un-
17 dermine them. *See Gonzalez*, 759 F.3d at 1115. For example, Goshert alleges that Plumb’s and the
18 Banfield Journal “indicate that Defendant’s product claims about the Supplements are false and mis-
19 leading.” Compl. ¶ 13. But the only inference to be drawn from these sources—as quoted directly in
20 the Complaint—is that glucosamine and chondroitin supplements’ efficacy is unsubstantiated. *See id.*
21 ¶ 13; Ex. 1 Att. A (Plumb’s) at 429 (“These compounds may be useful in treating osteoarthritis or other
22 painful conditions in domestic animals, but large, well-designed controlled clinical studies proving
23 efficacy were not located.”; “[w]ell tolerated, but efficacy is uncertain”); *id.* Att. B (Banfield) at 3
24 (stating as its “clinical bottom line” that “the benefits of using a combination of glucosamine hydro-
25 chloride and chondroitin sulfate nutraceuticals to improve symptoms associated with canine and feline
26 joint disease has yet to be determined.”; “[S]trong clinical evidence of efficacy is lacking, and these
27 compounds are understudied.”).

28 Both the Scott and Moreau studies also cautioned against drawing any global conclusions from

1 their results. *See* Ex. 1 Att. D (Scott) at 321 (declining to “comment on [glucosamine’s] overall effica-
2 cy given the limited number of dogs (n = 30) and duration of treatment (90 days)” and recognizing that
3 “differences [in studies] make it difficult to draw an all-encompassing conclusion regarding [glucosa-
4 mine] products safety and efficacy in dogs”); *id.* Att. C (Moreau) at 327 (“The recommended therapeu-
5 tic dose of CS-G-M may have been insufficient to provide a clinical improvement, and larger doses or
6 modifications to the proportions of its constituents may help to make it more effective, possibly in
7 dogs with less severe osteoarthritis.”). At bottom, Goshert’s “inconclusive, rather than contradictory,
8 evidence is not sufficient to state a claim.” *Bronson*, 2013 WL 1629191, at *8.

9 As for “anecdotal” evidence of falsity, *King Bio*, 107 Cal. App. 4th at 1348, Goshert fails to
10 allege that the Soft Chews had no impact on her dog, admitting elsewhere that she “is unable to deter-
11 mine if the Supplements are actually effective at helping her dog maintain and improve joint health.”
12 Compl. ¶¶ 16, 18. When parsed, Goshert’s evidence supports only an unactionable lack of substantia-
13 tion claim.

14 **C. Goshert also fails to state a claim under the UCL’s “unlawful” prong.**

15 Goshert’s claim under the UCL’s “unlawful” prong, which provides for a separate theory of
16 liability, *Lozano v. AT & T Wireless Servs., Inc.*, 504 F.3d 718, 731 (9th Cir. 2007), fails for similar
17 reasons. *See* Compl. ¶¶ 57–58. Under the unlawful prong, the UCL “borrows violations of other laws
18 and treats them as unlawful practices that the unfair competition law makes independently actionable.”
19 *De La Torre v. CashCall, Inc.*, 854 F.3d 1082, 1085 (9th Cir. 2017) (citation omitted). For this reason,
20 “a claim under this prong hinges upon whether a plaintiff can formulate a claim under the predicate
21 law.” *Eidmann v. Walgreen Co.*, 522 F. Supp. 3d 634, 647 (N.D. Cal. 2021); *see also Hadley v.*
22 *Kellogg Sales Co.*, 243 F. Supp. 3d 1074, 1094 (N.D. Cal. 2017).

23 Goshert predicates this claim on CLRA and FAL violations, and breach of implied warranty
24 (Counts I–II and V). Compl. ¶ 57. Goshert cannot state a claim under the predicate causes of action, so
25 her UCL unlawful claim fails. *See supra* at 4–8; *infra* at 15–17; *see, e.g., Punian v. Gillette Co.*, 2016
26 WL 1029607, at *17 (N.D. Cal. Mar. 15, 2016) (“Because the Court finds that Plaintiff did not
27 plausibly allege any statutory violations [under the CLRA and FAL], the Court also finds that Plaintiff
28 fails to plausibly allege violation of the unlawful prong of the UCL.”); *In re Google Phone Litig.*, 2012

1 WL 3155571, at *11 (N.D. Cal. Aug. 2, 2012) (finding plaintiff failed to state a claim under the UCL’s
2 unlawful prong when plaintiff failed to sufficiently plead predicate claims for breach of implied
3 warranty and violation of the CLRA).

4 Goshert’s UCL unlawful claim based on breach of implied warranty fails for another reason:
5 Goshert did not rely on the statements underlying this claim. Claims arising under the UCL’s unlawful
6 prong “require reliance when the underlying misconduct involves misrepresentation or deception.”
7 *Lanovaz*, 2014 WL 46822, at *2; *see also Kwikset Corp. v. Superior Court*, 246 P.3d 877, 888 (Cal.
8 2011) (requiring reliance for all three UCL prongs when the claims were based on false advertising
9 and misrepresentations). Goshert’s unlawful claim requires reliance because her allegations—that
10 Compana “tricked” consumers “into believing that the Supplements are fit for their purpose as joint
11 health supplements,” Compl. ¶ 60, “rely on the exact same set of facts and theory of liability or unified
12 course of conduct” as her misrepresentation claims. *Loh v. Future Motion, Inc.*, 2022 WL 2668380, at
13 *5 (N.D. Cal. July 11, 2022) (analyzing breach of implied warranty claim under Rule 9(b)’s pleading
14 requirements). Goshert alleges that Compana breached the implied warranties that the Soft Chews
15 would (a) pass without objection in the trade under the contract description and (b) were not fit for the
16 ordinary purposes for which such goods because the Soft Chews do not “maintain healthy bone and
17 joint function” and “maintain cartilage and connective tissue.” Compl. ¶ 78. But these two statements
18 were made on Doggie Dailies website, *see id.* ¶ 3, and Goshert does not allege that she relied on these
19 statements before purchasing the Soft Chews, *see id.* ¶ 16. Goshert’s failure to allege reliance dooms
20 these claim.

21 **D. Goshert’s equitable relief claims under the CLRA, FAL, and UCL fail as a matter**
22 **of law because Goshert has an adequate remedy at law.**

23 Goshert’s equitable relief claims under the CLRA, FAL, and UCL fail because Goshert does
24 not (and cannot) allege an inadequate remedy at law. Compl. ¶¶ 43, 51, 65; Prayer for Relief ¶¶ E–F.
25 Goshert’s claims for injunctive relief and restitution under the FAL and UCL and for injunctive relief
26 under the CLRA are equitable. *Nationwide Biweekly Admin., Inc. v. Superior Court of Alameda Cty.*,
27 462 P.3d 461, 488 9 Cal. 5th 279, 336 (Cal. 2020) (confirming that “civil causes of action authorized
28 by the UCL and FAL must properly be considered equitable, rather than legal, in nature”); *see also*

1 *Durkee v. Ford Motor Co.*, 2014 WL 4352184, at *3 (N.D. Cal. Sept. 2, 2014) (holding that CLRA in-
2 junctive relief is equitable). To bring claims equitable relief claims, the Ninth Circuit requires a party
3 to “sufficiently allege a lack of legal remedy in order to survive a motion to dismiss,” which Goshert
4 does not (and cannot) do here. *Barrett v. Apple Inc.*, 523 F. Supp. 3d 1132, 1157 (N.D. Cal. 2021) (cit-
5 ing *Sonner v. Premier Nutrition Corp.*, 971 F.3d 834, 844 (9th Cir. 2020)). In fact, Goshert admits to
6 an adequate legal remedy by seeking money damages for her CLRA, breach of warranty, and fraud
7 claims. Compl. ¶¶ 43, 84, 90; Prayer for Relief ¶ C; see *Williams v. Apple, Inc.*, 2020 WL 6743911, at
8 *9 (N.D. Cal. Nov. 17, 2020) (“Monetary damages are a remedy at law.” (citing *eBay Inc. v. Mer-*
9 *cExchange, L.L.C.*, 547 U.S. 388, 391 (2006))). Courts routinely dismiss equitable relief claims under
10 the CLRA, UCL, and FAL when the plaintiff has an adequate remedy at law. See, e.g., *In re California*
11 *Gasoline Spot Mkt. Antitrust Litig.*, 2021 WL 1176645, at *7 (N.D. Cal. Mar. 29, 2021) (Corley, J.)
12 (dismissing UCL claim because plaintiff “failed to allege that she lacked an adequate remedy at law”);
13 *Zapata Fonseca v. Goya Foods Inc.*, 2016 WL 4698942, at *7 (N.D. Cal. Sept. 8, 2016) (dismissing
14 claims for equitable relief under the CLRA, UCL, and FAL because plaintiff pled five other claims
15 which presented her with an adequate remedy at law); *In re MacBook Keyboard Litig.*, 2020 WL
16 6047253, at *4 (N.D. Cal. Oct. 13, 2020) (dismissing claims that “seek an injunction, restitution, or
17 other equitable relief” with prejudice); *Williams*, 2020 WL 6743911, at *9 (“[A] federal court cannot
18 grant relief under the UCL or FAL if Plaintiffs have an adequate remedy at law.”).

19 **E. Goshert’s CLRA claim must be dismissed as to the product and specific**
20 **representations for which she failed to provide pre-suit notice.**

21 Goshert’s CLRA claims for the 5-in-1 Multivitamin Soft Chews for Dogs and for the
22 statements “Promotes Cartilage Development” and “Specifically Formulated to Support Joint
23 Function” about the Soft Chews must be dismissed because Goshert failed to provide pre-suit notice.
24 Compl. ¶¶ 1, 16. Under Cal. Civ. Code § 1782(a), to seek damages under the CLRA, a plaintiff must
25 provide notice to the defendant of “the particular alleged violations” of the statute. The purpose of the
26 CLRA’s notice requirement is “to provide and facilitate precomplaint settlements of consumer actions
27 wherever possible and to establish a limited period during which such settlement may be
28 accomplished.” *Outboard Marine Corp. v. Super. Ct.*, 52 Cal. App. 3d 30, 41, 124 Cal. Rptr. 852

(1975). “Courts require strict compliance with the notice requirement in order to further this purpose.” *Ruszecki v. Nelson Bach USA Ltd.*, 2015 WL 6750980, at *5 (S.D. Cal. June 25, 2015). “[W]here a plaintiff brings a CLRA cause of action, damages claims for any product not specifically noticed must be dismissed.” *Sotelo v. Rawlings Sporting Goods Co., Inc.*, 2019 WL 4392528, at *6 (C.D. Cal. May 8, 2019) (collecting cases and dismissing claims for products that were not expressly identified in the CLRA notice). The same result applies for specific statements—i.e., the alleged violations—not noticed. *See Ruszecki*, 2015 WL 6750980, at *5.

Goshert’s counsel notified Compana of this lawsuit on July 11, 2022.⁶ Compl. ¶¶ 43, 71. That letter identified three Doggie Dailies products: “Doggies Dailies Advanced Hip & Joint Supplement for Dogs, Doggie Dailies Senior Essentials Advanced Hip & Joint, and Doggies Dailies Senior Essentials 10-in-1 Senior Multivitamin.” *See* Ex. 1 Att. E at 1 n.1 The letter did not identify the 5-in-1 Multivitamin Soft Chews for Dogs. As for specific representations made by Compana about the Soft Chews that violate allegedly California law, Goshert identified two: “Promotes Healthy Joints, Comfort, and Mobility” and “Doggie Dailies is a safe and effective hip and joint soft chew your dog will love. Our glucosamine dog treats are specially formulated to help promote healthy joints, mobility, and flexibility. A daily dose of Doggie Dailies soft chews can help support your dog’s mobility and overall joint health.” *Id.* The Notice Letter did not identify the two other statements that she also allegedly relied on—“Promotes Cartilage Development” and “Specifically Formulated to Support Joint Function.” Compl. ¶ 16. Goshert’s CLRA claim must therefore be dismissed as to the 5-in-1 Multivitamin Soft Chews for Dogs and these two statements about the Soft Chews.⁷ *See Ruszecki*, 2015 WL 6750980, at *6 (dismissing claims based on products and statements that were not identified

⁶ A copy of the June 11, 2022 demand letter is attached as Attachment E to Exhibit 1. The Court may consider this document under the incorporation by reference doctrine because Goshert alleges the contents of the letter in the Complaint. Compl. ¶¶ 43, 71. *See Davis*, 691 F.3d at 1160; *see, e.g., Coheso, Inc. v. Can’t Live Without It, LLC*, 2017 WL 10434396, at *1 n.1 (N.D. Cal. Dec. 18, 2017) (considering letter incorporated by reference into complaint on motion to dismiss). Or the Court may take judicial notice of this document. *See Spindler v. Gen. Motors, LLC*, 2022 WL 2905232, at *6 (N.D. Cal. July 21, 2022) (taking judicial notice of demand letter under Federal Rule of Evidence 201 because its “accuracy cannot reasonably be questioned”).

⁷ Goshert’s CLRA claim based on these statements and the 5-in-1 Multivitamin therefore cannot also constitute the predicate act for the UCL’s unlawful prong. *See supra* at 10–11.

1 in the notice letter); *Allen v. Similasan Corp.*, 2013 WL 5436648, at *3 (S.D. Cal. Sept. 27, 2013)
2 (same).

3 For all these reasons, Counts I, II, and III fail to state a claim and should be dismissed.

4 **II. Goshert fails to state a claim for breach of express warranty because she does not**
5 **plausibly allege breach or injury (Count IV).**

6 Goshert’s breach of express warranty claim fails for three reasons. Under Cal. Com. Code
7 § 2313, an express warranty is created through “[a]ny affirmation of fact or promise made by the seller
8 to the buyer which relates to the goods and becomes part of the basis of the bargain creates an express
9 warranty that the goods shall conform to the affirmation or promise.” To state a claim for breach of
10 express warranty under California law, Goshert must allege “(1) the exact terms of the warranty; (2)
11 reasonable reliance thereon; and (3) a breach of warranty which proximately caused plaintiff’s injury.”
12 *T & M Solar & Air Conditioning, Inc. v. Lennox Int’l Inc.*, 83 F. Supp. 3d 855, 875 (N.D. Cal. 2015)
13 (Corley, J.) (quoting *Minkler v. Apple, Inc.*, 65 F. Supp. 3d 810, 817 (N.D. Cal. 2014)). “To allege
14 facts identifying the exact terms of the warranty, a plaintiff must provide ‘specifics’ about what the
15 warranty statement was, and how and when it was breached.” *Id.* Goshert must also allege that she no-
16 tified Compana of the alleged breach to allow Compana “an opportunity to cure the defect outside of
17 court.” *Id.* (citing *Alvarez v. Chevron Corp.*, 656 F.3d 925, 932 (9th Cir. 2011); *see also* Cal. Com.
18 Code § 2607(3)(A) (stating that a buyer “must, within a reasonable time after he or she discovers or
19 should have discovered any breach, notify the seller of the breach or be barred from any remedy”).

20 *First*, Goshert’s breach of express warranty claim must be dismissed because Goshert has
21 failed to allege that the Statements are false or misleading under Rule 8 and Rule 9(b). *See supra* at 4–
22 8; *see, e.g., Loh*, 2022 WL 2668380, at *5 (dismissing CLRA, UCL, FAL, breach of implied warranty,
23 breach of express warranty, and unjust enrichment claims under Rule 9(b) together because they “all
24 rely on the exact same set of facts and theory of liability or unified course of conduct”); *Arabian v.*
25 *Organic Candy Factory*, 2018 WL 1406608, at *7–*8 (C.D. Cal. Mar. 19, 2018) (dismissing breach of
26 express warranty for failure to plead with Rule 9(b)’s required particularity when claims arose from
27 the defendant’s product’s alleged misrepresentation).

28 *Second*, Goshert fails to plausibly allege a breach of warranty that proximately caused her inju-

1 ry—“how and when” the express warranty was breached. *T & M Solar, Inc.*, 83 F. Supp. 3d at 875. A
2 breach of express warranty claim will require proof that “the product did not perform as stated or
3 promised.” *Deitsch Plastics Co., Inc. v. Gredale LLC*, 2022 WL 1449126, at *4 (C.D. Cal. May 6,
4 2022). Yet Goshert cannot plausibly allege that the Soft Chews did not perform as promised, admitting
5 that she is “unable to determine” if the Soft Chews are “actually effective at helping her dog maintain
6 and improve joint health.” Compl. ¶¶ 16, 18. And besides, the conclusory allegation that a product
7 “does not work” does not plausibly allege injury. *Eckler*, 2012 WL 5382218, at *8.

8 *Third*, if the court does not dismiss Goshert’s breach of express warranty claim outright, it
9 must be dismissed as to the statements “helps maintain healthy bone and joint function” and “cartilage
10 and connective tissue” for lack of reliance and failure to provide pre-suit notice. Compl. ¶¶ 68–70.
11 These two statements were made on Doggie Dailies website, *id.* ¶ 3, and Goshert does not allege that
12 she relied on these statements before purchasing the Soft Chews, *id.* ¶ 16; *see T & M Solar*, 83 F.
13 Supp. 3d at 875–76. Nor did Goshert notify Compana that these statements underlie her breach of ex-
14 press warranty claim. *Compare id.* ¶ 71, with Ex. 1 Att. E at 1. For the same reason, the 5-in-1 Multi-
15 vitamin Soft Chews for Dogs, which were unidentified in the Notice Letter, cannot underlie her breach
16 of express warranty claim either. *See* Ex. 1 Att. E at 1 n.1.

17 **III. Goshert fails to state a claim for breach of implied warranty under the Song-Beverly**
18 **Consumer Warranty Act and Cal. Comm. Code § 2314 (Count V).**

19 Goshert’s claim for breach of implied warranty under the Song-Beverly Consumer Warranty
20 Act and Cal. Comm. Code § 2314 fail for similar reasons. Compl. ¶¶ 72–84. “To state a viable claim
21 under California’s Song-Beverly Consumer Warranty Act, a plaintiff must plead sufficiently a breach
22 of warranty under California law.” *Baltazar v. Apple, Inc.*, 2011 WL 588209, at *3 (N.D. Cal. Feb. 10,
23 2011); *Birdsong v. Apple, Inc.*, 590 F.3d 955, 958 n.2 (9th Cir. 2009). Goshert premises her breach of
24 implied warranty claim on Cal. Comm. Code § 2314, which provides that for goods to be merchanta-
25 ble they must “[p]ass without objection in the trade under the contract description” and be “fit for the
26 ordinary purposes for which such goods are used.” *See* Compl. ¶ 78. The warranty of merchantability
27 “provides for a minimum level of quality.” *Birdsong*, 590 F.3d at 958 (citation omitted). “A plaintiff . .
28 . must show that the product did not possess even the most basic degree of fitness for ordinary use.”

1 *Swearingen v. Amazon Pres. Partners, Inc.*, 2014 WL 3934000, at *1 (N.D. Cal. Aug. 11, 2014); *Rose*
2 *v. HP Inc.*, 2020 WL 7714532, at *2 (N.D. Cal. Dec. 29, 2020) (“The warranty does not impose a gen-
3 eral requirement that goods precisely fulfill the expectation of the buyer.”) (cleaned up).

4 Goshert’s breach of implied warranty claim must be dismissed because Goshert’s allegations
5 about the Statements fail Rule 8’s plausibility standard and Rule 9(b)’s particularity requirement. *See*
6 *supra* at 4–8; *see Taleshpour v. Apple Inc.*, 2021 WL 1197494, at *7 (N.D. Cal. Mar. 30, 2021) (apply-
7 ing Rule 9(b) to breach of implied warranty claim); *see, e.g., Loh*, 2022 WL 2668380, at *5. Goshert
8 also cannot state a breach of implied warranty claim because she cannot plausibly allege that the Soft
9 Chews had no impact on her dog, admitting that she is “unable to determine” if the Soft Chews are
10 “actually effective at helping her dog maintain and improve joint health.” Compl. ¶¶ 16, 18; *see, e.g.,*
11 *Minkler*, 65 F. Supp. 3d at 819 (rejecting breach of implied warranty claim where Plaintiff failed to
12 allege that “Apple Maps failed to work at all or even that it failed to work a majority of the time”).

13 Goshert’s Song-Beverly Act claim also fails because the Soft Chews are exempted consuma-
14 bles. The Song-Beverly Act provides a right of action for buyers of “consumer goods” for implied
15 warranty violations, which is defined as “any new product or part thereof that is used, bought, or
16 leased for use primarily for personal, family, or household purposes, except for clothing and consuma-
17 bles.” Cal. Civ. Code §§ 1791(a), 1794. “Consumables” are defined as “any product that is intended
18 for consumption by individuals, or use by individuals for purposes of personal care or in the perfor-
19 mance of services ordinarily rendered within the household, and that usually is consumed or expended
20 in the course of consumption or use.” *Id.* § 1791(d). Courts routinely dismiss Song-Beverly Act claims
21 with prejudice when the product at issue is a “consumable” product.⁸

22 Here, the products at issue—dog supplements and multivitamins—are “consumables” under
23

24 ⁸ *See, e.g., Brazil v. Dole Food Co., Inc.*, 935 F. Supp. 2d 947, 965 (N.D. Cal. 2013) (dismissing Song-
25 Beverly Act claim because food products “are excluded from the Act”); *Kane v. Chobani, Inc.*, 2013
26 WL 5289253, *11 (N.D. Cal. Sept. 19, 2013) (dismissing Song-Beverly Act claims relating to yo-
27 gurts); *Smedt v. The Hain Celestial Grp., Inc.*, 2013 WL 4455495, *3 (N.D. Cal. Aug. 16, 2013)
28 (same); *Bishop v. 7-Eleven, Inc.*, 2013 WL 4014174, *3 (N.D. Cal. Aug. 5, 2013) (same); *Samet v.*
Procter & Gamble Co., 2013 WL 3124647, *10 (N.D. Cal. June 18, 2013) (dismissing Song-Beverly
Act claim because the products were “clearly products intended for consumption”); *Maxwell v. Unile-*
ver U.S., Inc., 2013 WL 1435232, *4 (N.D. Cal. Apr. 9, 2013) (finding food and beverage products
“fall under th[e] definition of ‘consumables’”).

1 the Song-Beverly Act. *See, e.g., Lytle*, 2019 WL 8060070, at *7 (dismissing Song-Beverly Act claim
2 for dog glucosamine/chondroitin supplements). Pet supplements and vitamins are for “use by individ-
3 uals . . . in the performance of services ordinarily rendered within the household”—feeding household
4 pets—and are “usually . . . consumed or expended in the course of consumption or use.” *Id.* The Dog-
5 gie Dailies products are thus exempted consumables under the Song-Beverly Act.

6 **IV. Goshert’s fraud claim (Count VI) should be dismissed because Goshert fails to satisfy the**
7 **heightened particularity required by Rule 9(b).**

8 Goshert’s claim for common law fraud clears neither Rule 8’s nor Rule 9(b)’s bar. First,
9 Goshert has not plausibly alleged a false statement by Compana, much less with sufficient particulari-
10 ty. *See supra* at 4–8; *see Kearns*, 567 F.3d at 1126 (listing elements of common law fraud). Without a
11 false statement, Goshert cannot state a claim for fraud under California common law. Nor has Goshert
12 plausibly alleged injury. *See supra* at 8–9; *see Kearns*, 567 F.3d at 1126. These faults alone should
13 result in Count VI’s dismissal under Rule 8’s plausibility standard or Rule 9(b)’s heightened particu-
14 larity standard.

15 On top of these fatal deficiencies, Goshert also fails to adequately plead scienter or intent to de-
16 fraud. *See Kearns*, 567 F.3d at 1126. Although Rule 9(b)’s heightened pleading requirement does not
17 apply to allegations of knowledge or intent, “*Twombly* and *Iqbal*’s pleading standards must still be ap-
18 plied to test complaints that contain claims of fraud.” *Eclectic Props. East, LLC v. Marcus & Mil-*
19 *lichap Co.*, 751 F.3d 990, 995 n.5 (9th Cir. 2014). This standard means that “[p]laintiffs must still
20 plead **facts** establishing scienter with the plausibility standard required under Rule 8(a).” *DeLeon v.*
21 *Wells Fargo Bank, N.A.*, 2011 WL 311376, at *8 (N.D. Cal. Jan. 28, 2011) (citing *Iqbal*, 556 U.S. at
22 686) (emphasis added); *see also Kumandan v. Google LLC*, 2022 WL 103551, at *11 (N.D. Cal. Jan.
23 11, 2022) (“Pleading scienter, including intent to defraud, requires more than conclusory allegations
24 and bare assertions amounting to nothing more than a formulaic recitation of the elements.”) (cleaned
25 up).

26 Goshert alleges no facts establishing Compana’s scienter or intent to defraud under Rule 8(a)’s
27 plausibility standard. In support of scienter and intent, Goshert can only muster that Compana is “un-
28 doubtedly aware” of the studies cited in the Complaint and “knows that the Supplements are ineffec-

1 tive.” Compl. ¶¶ 14, 88. Such “[c]onclusory allegations or formulaic recitation of the elements,” which
2 “are not entitled to the presumption of truth,” cannot support a fraud claim. *Strickland v. AT&T W.*
3 *Disability Benefits Program*, 2017 WL 3670784, at *2 (N.D. Cal. Aug. 24, 2017); *see also Adams v.*
4 *Johnson*, 355 F.3d 1179, 1183 (9th Cir. 2004) (“[U]nwarranted inferences are insufficient to defeat a
5 motion to dismiss.”); *see, e.g., Elgindy v. AGA Serv. Co.*, 2021 WL 1176535, at *14 (N.D. Cal. Mar.
6 29, 2021) (dismissing fraud claim because “the complaint contain[ed] only conclusory allegations that
7 Defendants knew or should have known”—without “any facts”—that consumers were being misled);
8 *Starcity Cap., LLC v. Bio-Matrix Sci. Grp., Inc.*, 2014 WL 851067, at *4 (S.D. Cal. Mar. 3, 2014) (re-
9 jecting plaintiff’s “conclusory allegations regarding Defendants’ knowledge of the falsity of the al-
10 leged misrepresentation”); *DeLeon*, 2011 WL 311376, at *8 (dismissing fraud claim supported only by
11 “conclusory allegations” about knowledge of falsity). Count VI must be dismissed.⁹

12 **V. Count VII for unjust enrichment claim must be dismissed.**

13 Goshert’s unjust enrichment claim must be dismissed for two reasons. *First*, Goshert’s unjust
14 enrichment claim fails to plausibly state a claim under Rule 8 and Rule 9(b). *See supra* at 4–8; *see,*
15 *e.g., Loh*, 2022 WL 2668380 at *5; *Punian*, 2016 WL 1029607, at *18 (dismissing unjust enrichment
16 claim “premised on the same factual allegations” as plaintiff’s CLRA, FAL, and UCL claims because
17 those claims failed).

18 *Second*, like the equitable relief sought under the CLRA, FAL, and UCL, Goshert does not
19 (and cannot) allege an inadequate remedy at law. *See supra* at 11–12; Compl. ¶¶ 93–95; Prayer for Re-
20 lief ¶ E. As an initial matter, “in California, there is not a standalone cause of action for unjust enrich-
21 ment.” *Astiana v. Hain Celestial Grp., Inc.*, 783 F.3d 753, 762 (9th Cir. 2015) (citation omitted). To be
22 sure, *Astiana* also held that “[w]hen a plaintiff alleges unjust enrichment, a court *may* construe the
23

24
25 ⁹ This analysis provides another reason for dismissing Goshert’s claim under the UCL’s fraudulent
26 prong. *See Kowalsky v. Hewlett-Packard Co.*, 771 F. Supp. 2d 1156, 1159–60, 1161 (N.D. Cal. 2011)
27 (“[C]ourts have been unwilling to impose liability under the fraudulent prong of the UCL when a de-
28 fendant lacked knowledge of the facts that rendered its representations misleading at the time it made
the representations.”) (cleaned up). And for dismissing Goshert’s claim under Section 1770(a)(9) of
the CLRA. *See* Compl. ¶ 41; *In re Sony PS3 Other OS Litig.*, 551 F. App’x 916, 921 (9th Cir. 2014)
 (“Section 1770(a)(9) is the only subsection that requires pleading fraud, since it specifically requires
intent to defraud, which, in turn, implies knowledge of the falsity.”) (citation omitted).

1 cause of action as a quasi-contract claim seeking restitution.” 783 F.3d at 762 (emphasis added). Yet
2 even “a quasi-contract claim cannot survive a motion to dismiss unless the proponent adequately
3 pleads that no legal remedy exists.” *Barrett v. Apple Inc.*, 523 F. Supp. 3d 1132, 1157 (N.D. Cal. 2021).
4 Goshert has an adequate remedy at law and does not plead otherwise, so her unjust enrichment claim
5 must be dismissed. *See, e.g., Zapata*, 2016 WL 4698942, at *7 (dismissing unjust enrichment claim
6 when plaintiff had an adequate remedy at law); *Barrett*, 523 F. Supp. 3d at 1157 (dismissing unjust en-
7 richment claim for failure to allege that there is no legal remedy); *Julian v. TTE Tech., Inc.*, 2020 WL
8 6743912, at *5 (N.D. Cal. Nov. 17, 2020) (same).

9 **VI. Goshert lacks standing to pursue injunctive relief and to assert claims for products that**
10 **she did not purchase.**

11 Goshert has failed to allege Article III standing to pursue injunctive relief and to represent pur-
12 chasers of the 5-in-1 Multivitamin for Soft Chews Dogs and the Advanced 10-in-1 Senior Multivita-
13 min, which she did not purchase. These claims should be dismissed under Rule 12(b)(1).

14 **A. Goshert lacks standing to pursue injunctive relief because Goshert has not**
15 **pleaded future injury.**

16 Goshert lacks standing under Article III to seek injunctive relief under the CLRA, FAL, and
17 UCL claims because Goshert fails to show “a sufficient likelihood that [s]he will again be wronged in
18 a similar way[.]” *City of Los Angeles v. Lyons*, 461 U.S. 95, 111 (1983); *see* Compl. ¶¶ 43, 51, 65;
19 Prayer for Relief ¶ F. To establish Article III standing, Goshert must allege the “irreducible constitu-
20 tional minimum of standing”: injury-in-fact, causation, and redressability. *Lujan v. Defs. of Wildlife*,
21 504 U.S. 555, 560 (1992). For injunctive relief, a prospective remedy, the threat of injury must be “ac-
22 tual and imminent, not conjectural or hypothetical.” *Summers v. Earth Island Inst.*, 555 U.S. 488, 493
23 (2009). In other words, the “threatened injury must be certainly impending to constitute injury in fact”
24 and “allegations of possible future injury are not sufficient.” *Clapper v. Amnesty Int’l USA*, 568 U.S.
25 398, 409 (2013) (cleaned up).

26 In *Davidson*, the Ninth Circuit held that in some cases, “a previously deceived consumer *may*
27 have standing to seek injunctive relief an injunction against false advertising or labeling.” 889 F.3d at
28 969 (emphasis added). There, the plaintiff purchased the defendant’s flushable wipes that were not in

fact flushable. *Id.* at 961–62. *Davidson* ultimately held that the plaintiff had Article III standing to seek injunctive relief because the plaintiff had “no way of determining whether the representation ‘flushable’ [was] in fact true” without first purchasing the wipes, and therefore, a “threatened injury” was still “certainly impending.” *Id.* at 972 (citation omitted). This conclusion was motivated by the Ninth Circuit’s determination that the plaintiff “face[d] the similar injury of being unable to rely on [defendant’s] representations of its product in deciding whether or not she should purchase the product in the future.” *Id.* at 971–72.

The concern in *Davidson* is irrelevant here. Goshert tries to steer her allegations within *Davidson*’s holding, alleging that she “continues to desire to purchase the Supplements for her dog from Defendant” and “understands that the composition of the Supplements may change over time.” Compl. ¶ 18. But these allegations do not square with the rest of Goshert’s Complaint. Goshert premises her claim that the Statements are false on two studies involving a different glucosamine and chondroitin product that is not alleged to contain the same concentration, combination, amount per dose, or directed dosage as the Soft Chews. Based on this, Goshert broadly concludes that *all* “supplements with glucosamine and chondroitin are ineffective for joint health in dogs.” Compl. ¶ 88; *see also id.* ¶ 7. For this reason, Goshert cannot “face[] the similar injury of being unable to rely on [Doggie Dailies’] representations of its product in deciding whether or not she should purchase the product in the future.” *Davidson*, 889 F.3d at 971–72. If the Soft Chews—or any other glucosamine and chondroitin supplement for that matter—still contain glucosamine and chondroitin, Goshert will know that they are “ineffective for joint health in dogs.” Compl. ¶ 88; *see, e.g., Cimoli v. Alacer Corp.*, 546 F. Supp. 3d 897, 907 (N.D. Cal. 2021) (distinguishing *Davidson* and finding plaintiff lacked standing because “[p]laintiff knows that he can determine the Products’ dosages by consulting the back labels”); *Shanks v. Jarrow Formulas, Inc.*, 2019 WL 7905745, at *5 (C.D. Cal. Dec. 27, 2019) (finding plaintiff lacked standing because “in the future [plaintiff can] simply look at the label on Defendant’s coconut oil . . . and put it back”). Goshert’s request for injunctive relief must be dismissed.

B. Goshert lacks standing to assert claims for purchasers of the Multivitamins because they are not substantially similar to the Soft Chews.

Goshert also lacks standing to assert claims involving the 5-in-1 Multivitamin Soft Chews for

1 Dogs and the Advanced 10-in-1 Senior Multivitamin (“Multivitamins”), which Goshert never pur-
2 chased.¹⁰ To begin with, Goshert lacks standing to represent purchasers of the Multivitamins because
3 Goshert cannot state a claim for her Soft Chews’ purchase. *See Hamm v. Mercedes-Benz USA, LLC*,
4 2022 WL 913192, at *4 (N.D. Cal. Mar. 29, 2022). Next, “[t]he majority of the courts that have careful-
5 ly analyzed the question hold that a plaintiff may have standing to assert claims for unnamed class
6 members based on products he or she did not purchase so long as the products and alleged misrepresen-
7 tations are substantially similar.” *Miller v. Ghirardelli Chocolate Co.*, 912 F. Supp. 2d 861, 869 (N.D.
8 Cal. 2012). To determine substantial similarity, “[c]ourts look to a series of factors including whether
9 the challenged products are of the same kind, comprised of largely the same ingredients, and whether
10 each of the challenged products bears the same alleged mislabeling.” *Figy v. Frito-Lay N. Am., Inc.*, 67
11 F. Supp. 3d 1075, 1083 (N.D. Cal. 2014).

12 Goshert lacks standing to assert claims involving the Multivitamins because she does not “al-
13 lege facts sufficient to show that there are substantial similarities between” the Soft Chews and the
14 Multivitamins. *Perez v. Bath & Body Works, LLC*, 2022 WL 2756670, at *7 (N.D. Cal. July 14, 2022).
15 Rather than include the Multivitamins’ labels, like Goshert did for the Soft Chews and the Senior Es-
16 sentials Advanced Hip & Joint Supplement for Senior Dogs, Compl. ¶¶ 3, 8, Goshert—perhaps recog-
17 nizing that the Multivitamins are dissimilar to the Soft Chews—makes only two allegations about the
18 Multivitamins: “Defendant claims that its 5-in-1 Multivitamins “[p]romotes strong, flexible joints”;
19 and “The website for Senior Essentials 10-in-1 Senior Multivitamin likewise states that the product
20 contains ‘glucosamine for joint health,’ and that it “[p]romotes strong bones & flexible joints.””
21 Compl. ¶¶ 4, 6. “Without additional details” about the Multivitamins, Goshert “has not satisfied her
22 burden to establish her standing to challenge” them. *Perez*, 2022 WL 2756670, at *7; *see, e.g., Kane*,
23 2013 WL 5289253, at *11 (requiring plaintiffs to “allege facts sufficient to show that the *products*
24 Plaintiffs did not purchase are ‘substantially similar’ to those that they did” on top of showing substan-
25 tial similarity for the misrepresentations) (emphasis in original); *Smedt v. Hain Celestial Group, Inc.*,
26 2014 WL 2466881, at *7 (N.D. Cal. May 30, 2014) (finding lack of information about “the products’
27

28 ¹⁰ Compana does not concede that Goshert has standing to bring claims for purchasers of the Senior
Essentials Advanced Hip & Joint Supplement for Senior Dogs.

1 respective ingredients or packaging showing how the unpurchased products are substantially similar to
2 the purchased products” prevented the court from “determin[ing] from the pleadings whether the
3 named products are, in fact, substantially similar to the purchased products”); *Wilson v. Frito-Lay N.*
4 *Am., Inc.*, 961 F. Supp. 2d 1134, 1141 (N.D. Cal. 2013) (refusing to assume that the non-purchased
5 products’ labels are actionable just like the more fully described purchased products’ labels when
6 plaintiffs “simply provide[d] a list of Non-Purchased Products, attach[ed] barely-legible labels . . . ,
7 and assert[ed] that these labels are unlawful or misleading”).

8 Goshert alleges so little because she cannot plausibly allege substantial similarity even if she
9 tried. Although Goshert collectively refers to the Doggie Dailies products as “Supplements,” that is
10 misleading. The Soft Chews and the Senior Essentials Advanced Hip & Joint Supplement for Senior
11 Dogs are hip & joint supplements; the 5-in-1 Multivitamin and 10-in-1 Senior Multivitamin are, as the
12 names imply, multivitamins—focusing on supporting dogs’ overall health. The 5-in-1 Multivitamin
13 contains “vitamins and minerals to complement [a] dog’s normal diet” to “Provide[] Antioxidant Sup-
14 port + Nutritional Support for Joints, Skin & Coat, Digestion, and The Immune System.”¹¹ Ex. 1 Att.
15 F. The 10-in-1 Senior Multivitamin are similarly “packed with a powerful blend of vitamins and min-
16 erals” to “Provide[] Antioxidants, Joint Support & Nutritional Support for Skin & Coat, Digestion,
17 Kidneys, Heart Function, Eye Function, Brain & The Immune System.”¹² See Compl. ¶ 6 n.8. And the
18 Multivitamins’ labels themselves each contain a single unrelated representation about joint support:
19 “Nutritional Support for Joints” (5-in-1 Multivitamin) and “Joint Support” (10-in-1 Senior Multivita-
20 min). See Ex. 1 Att. F; Compl. ¶ 6 n.8.

21
22 ¹¹ A copy of the 5-in-1 Multivitamin’s label is attached as Attachment F to Exhibit 1. The Court may
23 properly consider this Attachment under the incorporation by reference doctrine because the Com-
24 plaint cites and relies on the specific web page where this label is found. Compl. ¶ 4 n.5. See *Knievel*
25 *v. ESPN*, 393 F.3d 1068, 1076–77 (9th Cir. 2005) (considering web page incorporated by reference
26 where additional portions of the same web page were relevant to and incorporated by the plaintiffs’
27 allegations); *Daniels-Hall v. Nat’l Educ. Ass’n*, 629 F.3d 992, 998 (9th Cir. 2010) (considering infor-
28 mation posted on certain “web pages that Plaintiffs referenced in the Complaint”); *Arroyo, v. AJU Ho-
tel Silicon Valley LLC*, 2021 WL 2350813, at *2 (N.D. Cal. Mar. 16, 2021) (considering web pages
under the incorporation by reference doctrine because they are “document[s] whose contents are al-
leged in the complaint and on which the complaint necessarily relies”).

¹² The court may consider the 10-in-1 Senior Multivitamin web page because the Complaint cites and
relies on the specific web page where this information is found. See *supra* at 22 n.11.

The Multivitamins’ active ingredients list, which Goshert omits from the Complaint, shows its broad target. The 5-in-1 Multivitamin contains at least 31 active ingredients and the 10-in-1 Senior Multivitamin contains at least 30 active ingredients, while the Soft Chews contains only 8 active ingredients. *Compare* Ex. 1 Att. F, *and* Compl. ¶ 6 n.8, *with id.* ¶ 3 n.1. *See Dysthe v. Basic Rsch. LLC*, 2011 WL 5868307, at *4–*5 (C.D. Cal. June 13, 2011) (finding plaintiffs lacked standing for claims involving products with “significant differences” from the products they purchased, including that one product contained nineteen ingredients and the other contained ten). In fact, although Goshert alleges that all four Doggie Dailies products “contain[] the[] same key active ingredients”—“glucosamine hydrochloride and chondroitin sulfate”—that is not true. Compl. ¶¶ 7–8. The 5-in-1 Multivitamin contains no chondroitin. Ex. 1 Att. F. When a plaintiff groups product together based on the same combination of ingredients, and one of those products lacks the same combination, courts find that such product lacks substantial similarity. *See, e.g., Lytle*, 2019 WL 8060070, at *3 (dismissing claims against unpurchased products that did not have the glucosamine/chondroitin combination when claims were based on alleged ineffectiveness of those two key ingredients); *Yamasaki*, 2021 WL 4951435, at *3 (dismissing claims against unpurchased products that lacked zinc when allegations were based on zinc’s ineffectiveness in cold remedy products). At bottom, Goshert cannot proceed on her claims for Multivitamins’ purchasers. The Complaint does not plead enough facts establishing standing for these products, and any added information would highlight Goshert’s standing problem even more. The Complaint should be dismissed as to the 5-in-1 Multivitamin Soft Chews for Dogs and the Advanced 10-in-1 Senior Multivitamins.

CONCLUSION

Compana Pet Brands requests that the Court grant its motion to dismiss Goshert’s Class Action Complaint and grant any other relief that the Court deems just and proper under the circumstances of this case.

Dated this 15th day of September, 2022.

CERTIFICATE OF SERVICE

The undersigned hereby certifies that a copy of the foregoing was served via the Court's electronic notification system this 15th day of September, 2022 on all counsel of record.

s/ Jennifer Lee

EXHIBIT 1

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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA (SAN FRANCISCO)

LINDA GOSHERT, individually and on behalf of
all others similarly situated,

Plaintiff,

v.

COMPANA PET BRANDS,

Defendant

No.: 3:22-cv-04617-JSC

**DECLARATION OF JENNIFER LEE IN
SUPPORT OF MOTION TO DISMISS**

1 I, Jennifer Lee, hereby declare as follows:

2 1. I am an attorney at Husch Blackwell LLP, counsel for Defendant Compana Pet Brands
3 in this matter. I am a member in good standing of the state bar of California.

4 2. The facts set forth in this declaration are based upon my personal knowledge, and I
5 would competently testify to them if called upon to do so.

6 3. Attached as **Attachment A** to this declaration is a true and accurate copy of the entry
7 for “Glucosamine/Chondroitin Sulfate” available in DONALD C. PLUMB, PLUMB’S VETERI-
8 NARY DRUG HANDBOOK (6th ed. 2008). In Paragraph 13 of the Complaint, Plaintiff quotes and
9 cites this source.

10 4. Attached as **Attachment B** to this declaration is a true and accurate copy of Ashlee
11 Addleman, Evaluation of glucosamine hydrochloride/chondroitin sulfate nutraceuticals for treatment
12 of canine and feline joint disease, 6 Banfield J. 4 (2010). In Paragraph 13 of the Complaint, Plaintiff
13 partially quotes and cites this source.

14 5. Attached as **Attachment C** to this declaration is a true and accurate copy of Moreau,
15 M., et al., Clinical Evaluation Of A Nutraceutical, Carprofen And Meloxicam For The Treatment Of
16 Dogs With Osteoarthritis, Vet. Record No. 152 (2003). In Paragraph 10 of the Complaint, Plaintiff
17 partially quotes and cites this source.

18 6. Attached as **Attachment D** to this declaration is a true and accurate copy of Scott, R. et
19 al., Efficacy Of An Oral Nutraceutical For The Treatment Of Canine Arthritis: A Double-Blind Ran-
20 domized, Placebo-Controlled Prospective Clinical Trial, Vet. Comp. Ortho. Traumatol., 30 (2017). In
21 Paragraph 11 of the Complaint, Plaintiff partially quotes and cites this source.

22 7. Attached as **Attachment E** to this declaration is a true and accurate copy of a July 11,
23 2022 Notice and Demand Letter sent to Compana Pet Brands by L. Timothy Fisher of Bursor & Fish-
24 er, P.A.

25 8. Attached as **Attachment F** to this declaration is a true and accurate copy of the label
26 for Doggie Dailies 5-in-1 Multivitamin Soft Chews for Dogs located at
27 [https://www.amazon.com/Doggie-Dailies-Multivitamin-Improved-](https://www.amazon.com/Doggie-Dailies-Multivitamin-Improved-Digestion/dp/B07NSCLHK2/ref=sr_1_1_sspa?keywords=doggie%2Bdailies%2Bmultivitamin&q)
28 [Digestion/dp/B07NSCLHK2/ref=sr_1_1_sspa?keywords=doggie%2Bdailies%2Bmultivitamin&q](https://www.amazon.com/Doggie-Dailies-Multivitamin-Improved-Digestion/dp/B07NSCLHK2/ref=sr_1_1_sspa?keywords=doggie%2Bdailies%2Bmultivitamin&q)

1 [d=1659727264&prefix=doggie%2Bdailies%2Bmultiv%2Caps%2C148&sr=8-1-spons&th=1](https://www.dailymail.com/news/uk-politics/article-1659727264&prefix=doggie%2Bdailies%2Bmultiv%2Caps%2C148&sr=8-1-spons&th=1) (last
2 accessed September 10, 2022). In Paragraph 4 n.5 of the Complaint, Plaintiff cites this web page.

3
4 Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the above statements are
5 true and correct.

6
7 EXECUTED this 12th day of September, 2022.

8
9 Jennifer Lee
Jennifer Lee

ATTACHMENT A

Plumb's
**Veterinary
Drug
Handbook**

SIXTH EDITION

Donald C. Plumb

 **Blackwell**
Publishing

Plumb's
Veterinary Drug
Handbook

Sixth Edition

Donald C. Plumb, Pharm.D.

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Blackwell Publishing

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- **PHENOBARBITAL:** May increase the metabolism of glucocorticoids
- **PHENYTOIN:** May increase the metabolism of glucocorticoids
- **RIFAMPIN:** May increase the metabolism of glucocorticoids
- **VACCINES:** Patients receiving corticosteroids at immunosuppressive dosages should generally not receive live attenuated-virus vaccines as virus replication may be augmented; a diminished immune response may occur after vaccine, toxoid, or bacterin administration in patients receiving glucocorticoids

Laboratory Considerations

- Glucocorticoids may increase serum **cholesterol** and **urine glucose** levels.
- Glucocorticoids may decrease serum **potassium**.
- Glucocorticoids can suppress the release of thyroid stimulating hormone (TSH) and reduce **T₃** & **T₄** values. Thyroid gland atrophy has been reported after chronic glucocorticoid administration. Uptake of ¹³¹I by the thyroid may be decreased by glucocorticoids.
- Reactions to **skin tests** may be suppressed by glucocorticoids.
- False-negative results of the **nitroblue tetrazolium test for systemic bacterial infections** may be induced by glucocorticoids.

Monitoring

Monitoring of glucocorticoid therapy is dependent on its reason for use, dosage, agent used (amount of mineralocorticoid activity), dosage schedule (daily versus alternate day therapy), duration of therapy, and the animal's age and condition. The following list may not be appropriate or complete for all animals; use clinical assessment and judgment should adverse effects be noted:

- Weight, appetite, signs of edema
- Serum and/or urine electrolytes
- Total plasma proteins, albumin
- Blood glucose
- Growth and development in young animals
- ACTH stimulation test if necessary

Client Information

- Clients should carefully follow the dosage instructions and should not discontinue the drug abruptly without consulting with veterinarian beforehand.
- Clients should be briefed on the potential adverse effects that can be seen with these drugs and instructed to contact the veterinarian should these effects progress or become severe.

GLUCOSAMINE/CHONDROITIN SULFATE

(gloo-kose-a-meen/kon-droy-tin sul-fayt) Cosequin®

NUTRITIONAL SUPPLEMENT

Prescriber Highlights

- ▶ So-called nutraceutical that can be used as an adjunctive treatment for osteoarthritis or other painful conditions in horses, cats, dogs, etc; FLUTD in cats
- ▶ Well tolerated, but efficacy is uncertain
- ▶ Not a regulated drug; choose products carefully; large variation in commercially available products

Uses/Indications

These compounds may be useful in treating osteoarthritis or other painful conditions in domestic animals, but large, well-designed controlled clinical studies proving efficacy were not located. One study in dogs (McCarthy, O'Donovan et al. 2007) showed some positive effect, but this study was not placebo controlled and compared responses versus carprofen. Another placebo-controlled, blinded study in dogs (Moreau, Dupuis et al. 2003), did not demonstrate statistically significant improvement after 60 days of treatment.

These compounds potentially could be of benefit in cats with FLUTD (feline lower urinary tract disease) because of the presence of glycosaminoglycans as part of the protective layer of the urinary tract. Controlled studies have shown some positive effects in some cats, but overall did not appear to make a significant difference.

Pharmacology/Actions

Cartilage cells use glucosamine to produce glycosaminoglycans and hyaluronan. Glucosamine also regulates synthesis of collagen and proteoglycans in cartilage and has mild antiinflammatory effects due to its ability to scavenge free radicals. Chondrocytes normally produce ample quantities of glucosamine from glucose and amino acids, but this ability may diminish with age, disease, or trauma. Exogenously administered glucosamine appears to be able to be utilized by chondrocytes.

Chondroitin sulfate possesses several pharmacologic effects. It appears to inhibit destructive enzymes in joint fluid and cartilage. Thrombi formation in microvasculature may be reduced. In joint cartilage, it stimulates the production of glycosaminoglycans and proteoglycans.

While *in vitro* evidence exists, there is not solid evidence that using these compounds together improves clinical effect over either alone, but *in vivo* studies are ongoing.

Pharmacokinetics

The pharmacokinetics of these compounds are hard to evaluate due to the different salts, lack of standards, etc. Both glucosamine HCl and glucosamine sulfate are absorbed in the gut after the salt is cleaved in the stomach. There exists controversy as to whether either salt of glucosamine is superior to the other. Theoretically, if the amount of glucosamine base contained in the product is equivalent, the amount absorbed should be as well. Most clinical studies in veterinary species have been done with the HCl salt. Purified, low molecular weight chondroitin appears to be absorbed from the gut. Reported bioavailability in horses for chondroitin sulfate is about 25%; glucosamine, about 2%; bioavailability in dogs is reportedly about 5% for chondroitin sulfate and 12% for glucosamine.

Onset of any clinical efficacy may require 2–6 weeks of treatment.

Contraindications/Precautions/Warnings

No absolute contraindications were located for these compounds. As hypersensitivity reactions are a theoretical possibility, animals demonstrating prior hypersensitivity reactions to these compounds should not receive them.

In humans, glucosamine may exacerbate symptoms associated with asthma. Although this has not yet been reported in veterinary patients, caution is advised in patients with bronchoconstrictive conditions.

Adverse Effects

These products appear to be very well tolerated in dogs, cats, and horses. Adverse effects could potentially include some minor gastrointestinal effects (flatulence, stool softening). Since these products are often derived from natural sources, hypersensitivity reactions could occur.

Reproductive/Nursing Safety

No studies on the safety of these compounds in pregnant or lactating animals have been performed.

Overdosage/Acute Toxicity

Oral overdosage is unlikely to cause significant problems. The LD₅₀ for the combined compound in rats is greater than 5 g/kg. Gastrointestinal effects may result. Changes in coagulation parameters could occur, but have not been documented to date.

Products that contain manganese could lead to manganese toxicity if given in very high dosages (above label recommendations) chronically.

Drug Interactions

No clinically significant drug interactions have been reported to date. By reducing **doxorubicin** or **etoposide** inhibition of topoisomerase II, glucosamine may induce resistance to these agents. High dose chondroitin sulfate and/or glucosamine potentially could enhance the effects of **warfarin**, **heparin**, or other drugs that affect coagulation. Again, clinically significant interactions with either of these compounds have not been confirmed.

Laboratory Considerations

- High dose chondroitin and glucosamine theoretically could increase International Normalized Ratio (INR) in patients taking warfarin.

Doses

Note: Because of the variability in products available, it is recommended to choose a product that has been tested in the species for which it is marketed; consult the product label.

■ DOGS:

- a) For adjunctive treatment of chronic pain: Glucosamine/chondroitin: 13–15 mg/kg (of the chondroitin component) PO once daily (q24h). (Hardie, Lascelles et al. 2003)
- b) For adjunctive treatment of cancer pain: Glucosamine/chondroitin: 15–30 mg/kg (of the chondroitin component) PO once daily (q24h) for 4–6 weeks then half the dose. (Lascelles 2003)
- c) For adjunctive treatment of chronic pain: Glucosamine/chondroitin: 13–15 mg/kg (of the chondroitin component) PO once daily or every other day (q24–48h). (Hansen 2003b)
- d) Label Recommendation as a Dietary Supplement for *Cosequin*®:

For **Small Dogs** (under 25 lbs): Initially, using Regular Strength capsules for cats and small dogs: under 10 lb.: ½ to 1 capsule daily; 10–24 lb.: 2 capsules daily (1 in AM/ 1 in PM). Maintenance Administration (after initial 4–6 week period): under 10 lb. can often have their dosage reduced to ½ capsule daily or 1 capsule every other day. 10 to 24 lb. can often have their dosage reduced to 1 capsule daily.

For **Medium and Large Dogs** (>25 lbs.): Initially, using *Cosequin*®DS (double strength) tablets or capsules: 25–49 lb.: 2 capsules daily (1 in AM/ 1 in PM); 50–100 lb.: 3 capsules daily (2 in AM/ 1 in PM); over 100 lb.: 4 capsules daily (2 in AM/ 2 in PM). Maintenance Administration (after initial 4–6 week period): dogs can have their total daily dosage gradually lowered until maintenance level is reached.

Amount can be increased at any time depending on the pet's needs. Tablets can be given as a treat or crumbled and mixed with the pet's food. The capsules can be pulled apart and the contents sprinkled on the pet's food. Wet or moist food works best. As an alternative, pets can be pill or the

capsules administered by wrapping in a small piece of food. (Label recommendations; *Cosequin*®—Nutramax)

■ CATS:

- a) For adjunctive treatment of cancer pain: Glucosamine/chondroitin: 15–30 mg/kg (of the chondroitin component) PO once daily (q24h) for 4–6 weeks then half the dose. (Lascelles 2003)
- b) For adjunctive treatment of chronic pain: Glucosamine/chondroitin: 15–20 mg/kg (of the chondroitin component) PO once daily or every other day (q24–48h). (Hansen 2003b)
- c) Label Recommendation as a Dietary Supplement for *Cosequin*® For Cats: Initially: under 10 lb.: 1 capsule sprinkled on food daily; over 10 lb.: 2 capsules sprinkled on food daily (1 in AM/ 1 in PM). Maintenance Administration (after initial 4–6 week period): once desired response is obtained, capsules may be administered every other day.

Number of capsules can be increased at any time depending on the pet's needs. The capsules contain a flavored powder. The capsules should be opened and the contents mixed with or sprinkled over the food. Dry food may be moistened with a small amount of water so that the powder sticks. Alternatively, the contents of the capsules may be mixed with a small amount (*i.e.*, tablespoon) of wet or moist food. As an alternative, cats can be pill. (Label recommendations; *Cosequin*® For Cats—Nutramax)

■ HORSES:

- a) For navicular syndrome: Using *Cosequin*® Concentrated Powder labeled for horses: 16.5 grams (5 scoops) in feed twice daily. (Hanson, Brawner et al. 2001)
- b) Label Recommendation as a Dietary Supplement for *Cosequin*® Concentrated Powder: Initially: for horses under 600 lb., 2 scoops in AM and 2 scoops in PM; horses 600–1,200 lb., 3 scoops in AM and 3 scoops in PM; horses over 1,200 lb., 4 scoops in AM and 4 scoops in PM. The initial administration period is 2 to 4 weeks; if horse shows little or no response, extend initial amount for two more weeks.

Transition Period: Do not lower amount until horse has begun to respond. After achieving a good response, reduce total daily amount by one level scoop each week. Gradually reducing the amount will help find an individual maintenance level. Suggested Maintenance Administration: horses under 600 lb., 1 scoop daily; horses 600–1,200 lb., 1–2 scoops daily; horses over 1,200 lb., 2 scoops daily. Amount can be increased at any time.

May be top dressed on sweet feed. Add a small amount of water or molasses to get the powder to stick to dry feed. (Label and insert recommendations; *Cosequin*® Concentrated Powder—Nutramax Labs)

Monitoring

- Clinical efficacy

Client Information

- Onset of any clinical improvement may require 2–6 weeks of treatment.
- Do not switch brands from that prescribed without first contacting your veterinarian.
- Side effects are unlikely, but mild gastrointestinal upset has been reported in small animals. Should this be troublesome, contact your veterinarian.

Chemistry/Synonyms

Glucosamine is most often available as either glucosamine HCl or glucosamine sulfate. It is an amino sugar that is synthesized *in vivo* by animal cells from glucose and glutamine.

Glucosamine (HCl or Sulfate) may also be known as: chitosamine, NSC-758, 2-amino-2-deoxy-beta-D-glucopyranose, G6SD-glucosamine, glucose-6-phosphate, or amino monosaccharide.

Chondroitin sulfate is an acid mucopolysaccharide/glycosaminoglycan that is found in most cartilaginous tissues. It is a long chain compound that contains units of galactosamine and glucuronic acid.

Chondroitin sulfate may also be known as chondroitin 4-sulfate, chondroitin sulfate A, chondroitin sulfate B, chondroitin sulfate C, chondroitin sulfate sodium, CSA, sodium chondroitin sulfate, chondroitin polysulfate, CDA, CSCSC, GAG, or galactosaminoglycan sulfate.

Storage/Stability

Because of the multiple products and product formulations available, check label for storage and stability (expiration date) information. Chondroitin sulfate is an extremely hygroscopic compound and, generally, these products should be stored in tight containers at room temperature. Avoid storing in direct sunlight.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

None as pharmaceuticals. Supplements are available from a wide variety of sources and dosage forms include tablets, capsules and powder in a variety of concentrations. There are specific products marketed for use in animals, including *Cosequin*®, *Restor-A-Flex*®, *OsteO-3*®, *Arthri-Nu*®, *ProMotion*®, *Seraquin*®, *Oste-O-Guard*®, *Caniflex*®, *Equi-Phar Flex*®, etc.

Glucosamine and chondroitin sulfate are considered nutritional supplements by the FDA. No standards have been accepted for potency, purity, safety or efficacy by regulatory bodies.

Bioequivalence between products cannot be assumed and independent analysis has shown a wide variation in products.

HUMAN-LABELED PRODUCTS: None as pharmaceuticals

GLUTAMINE

(gloo-ta-meen)

NUTRITIONAL

Prescriber Highlights

- ▶ Amino acid that may be useful in preventing/treating GI epithelium damage
- ▶ Little documentation for efficacy, but adverse effects unlikely

Uses/Indications

Glutamine has been used as a GI protectant and in an attempt to enhance GI healing in conditions where GI epithelium is damaged (Parvo enteritis, chemotherapy, etc.).

A study that evaluated the efficacy of glutamine supplementation in cats with methotrexate-induced enteritis found no difference between cats supplemented with glutamine and those that were not. (Marks, Cook et al. 1999)

Pharmacology/Actions

Glutamine is a conditionally essential amino acid that is produced primarily in skeletal muscle and then released into the circulation. Glutamine is required for proper function of the immune system, GI tract, kidneys, and liver. Glutamine also serves as a precursor for glutathione, glutamate, purines, pyrimidines, and other amino acids.

Glutamine's effects on the gastrointestinal tract are one of the primary areas of interest for its therapeutic use as an exogenously administered drug. When the body is under severe stress, it consumes more glutamine than it can produce and progressive muscle wasting occurs as it tries to meet glutamine requirements. There is some evidence that glutamine may have a role in intestinal cell proliferation and determination. When glutamine is depleted, intestinal epithelium can atrophy, ulcerate, or become necrotic. In patients undergoing cancer chemotherapy or radiotherapy, diminished glutamine levels in the gastrointestinal tract can cause increased GI toxicity. Supplementation of exogenous glutamine may help protect the GI from these effects.

Pharmacokinetics

Little information was located outside of what is described in the pharmacology section.

Contraindications/Precautions/Warnings

Because it is partially metabolized into ammonia and glutamate, use with caution in patients with severe hepatic insufficiency, severe behavior disorders or epilepsy.

Adverse Effects

Glutamine is well tolerated when used orally or intravenously. Potentially, it may have some CNS effects at high dosages.

Reproductive/Nursing Safety

There is insufficient data available documenting the safe use of glutamine during pregnancy or nursing.

Overdosage/Acute Toxicity

Overdosages are unlikely to be harmful. Doses of up to 40 grams per day IV have been tolerated in humans without ill effects. Because glutamine is partially metabolized to ammonia, patients with hepatic insufficiency may be adversely affected.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving glutamine and may be of significance in veterinary patients:

- **ANTICONSULSANT MEDICATIONS:** Glutamine could potentially affect the efficacy of antiseizure medications (**phenobarbital**, **potassium bromide**, etc.). It is partially converted into glutamate, which can act as an excitatory neurotransmitter.
- **LACTULOSE:** Theoretically, glutamine may antagonize the effects of lactulose in patients with hepatic encephalopathy.

Laboratory Considerations

- Glutamine may increase **serum ammonia** or **glutamate** levels.

Doses

■ DOGS & CATS:

For adjunctive treatment of GI inflammatory conditions:

- a) 0.5 grams/kg PO daily (Wynn 2002)
- b) 0.5 gram/kg/day PO divided twice a day in the water or food. (Silverstein 2003)

ATTACHMENT B

CRITICALLY APPRAISED TOPIC:

Evaluation of glucosamine hydrochloride/ chondroitin sulfate nutraceuticals as a treatment to improve symptoms associated with canine and feline joint disease

Despite some evidence that a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals improves symptoms associated with joint disease in dogs and cats, strong clinical evidence of efficacy is lacking, and these compounds are understudied.

**BY ASHLEE ADDLEMAN, MPH
CONTRIBUTING AUTHOR**

CLINICAL QUESTION

Does a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals (*i.e.*, chondroprotectants) improve symptoms associated with joint disease in dogs and cats?

CLINICAL BOTTOM LINE

The limited number of high quality clinical trials and the lack of data on objective measures of efficacy preclude recommendations of glucosamine hydrochloride and chondroitin sulfate nutraceuticals as a sole medical treatment for joint disease in dogs and cats.¹⁻³

In brief, the benefits of using a combination of glucosamine hydrochloride and chondroitin sulfate nutraceuticals to improve symptoms associated with canine and feline joint disease has yet to be determined.

EVIDENCE SUMMARY**PubMed database search details
(January 2000 through current):**

- Canine: ("glucosamine"[MeSH Terms] OR "glucosamine"[All Fields]) AND ("chondroitin"[MeSH Terms] OR "chondroitin"[All Fields]) AND ("dogs"[MeSH Terms] OR "dogs"[All Fields]) OR

"canine"[All Fields]) AND ("arthritis"[MeSH Terms] OR "arthritis"[All Fields])

- Feline: ("glucosamine"[MeSH Terms] OR "glucosamine"[All Fields]) AND ("chondroitin"[MeSH Terms] OR "chondroitin"[All Fields]) AND ("felidae"[MeSH Terms] OR "felidae"[All Fields]) OR "feline"[All Fields]) AND ("arthritis"[MeSH Terms] OR "arthritis"[All Fields])
- Animals: ("glucosamine"[MeSH Terms] OR "glucosamine"[All Fields]) AND ("chondroitin"[MeSH Terms] OR "chondroitin"[All Fields]) AND ("animals"[MeSH Terms:noexp] OR animals[All Fields])

MAIN RESULTS

Veterinary clinical trials evaluating the efficacy, the duration of effect and absorption of glucosamine hydrochloride and chondroitin sulfate nutraceuticals are limited and results are conflicting to some extent.^{1,2,4,5}

The purity and quality of these compounds vary widely in commercial supplements.^{2,4}

Assessments of the safety of these products for dogs and cats are scarce, but some evidence shows that there are few side effects associated with either short or long term use.^{3,6}

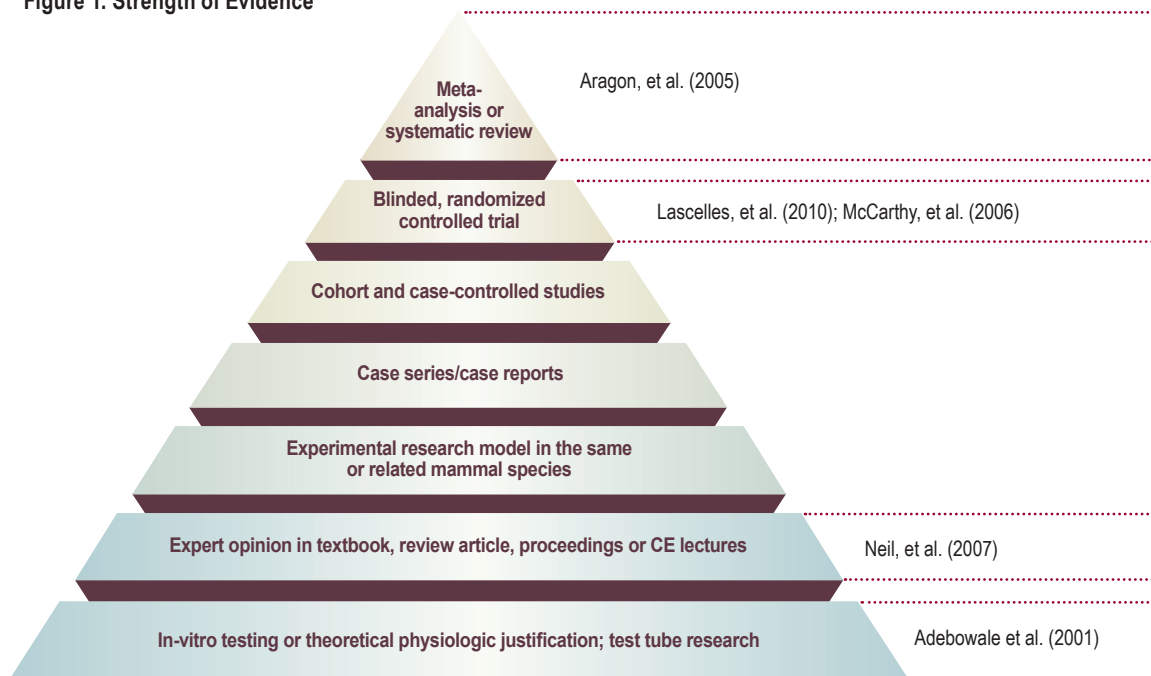
A few *In vitro* studies show beneficial effects and support the chondroprotective effect.²

Some evidence exists that diets supplemented with green-lipped mussel extract, glucosamine hydrochloride and chondroitin sulfate improves mobility in cats with joint disease.⁷

Bioavailability and pharmacokinetic data, although

limited, suggest that when combined, the compounds are absorbed in dogs and that there is accumulation after multiple dosing, suggesting a possible residual effect. This is consistent with *in vitro* studies and the two compounds may therefore be more beneficial when used together.^{2, 8}

Figure 1: Strength of Evidence*



*See corresponding Evidence Summary, Table 1, page 5.

COMMENTS

- The studies reviewed for this report mainly included dogs as study participants (n=4); one study involved cats as study participants and one systematic review included both.
- Most efficacy studies involving the combination of the two compounds are conducted with humans—extrapolating from these studies, it is recommended to use these nutraceuticals for Pets with mild to moderate joint disease.^{1,2,7,8}
- Mechanism of action and pharmacokinetics of these compounds in dogs and cats requires further investigation as the evidence is incomplete or lacking^{2,7,8}
- Future research is needed to establish objective measurements for joint disease symptoms, mobility and pain for use by veterinarians (e.g., force plate gait analysis, accelerometers, validated pain scale).⁴
- Additionally, a validated owner questionnaire is

needed in order to evaluate joint disease associated pain at home.⁷

- Currently, dosages are most likely extrapolated from studies involving other species.^{3,4} Further studies are necessary to determine how purity, source and composition affect efficacy of glucosamine hydrochloride and chondroitin sulfate preparations in veterinary patients.^{3,4}
- Beneficial effect and bioavailability have yet to be established for glucosamine hydrochloride and chondroitin sulfate when included in manufactured pet food.^{5,7}
- Rigorously designed long-term trials, using objective outcome assessments, to examine the effectiveness of glucosamine hydrochloride and chondroitin sulfate nutraceuticals in cats and dogs are needed.^{1,2,7}

CAT Appraiser: Ashlee Addleman, MPH

Date CAT was “born”/expiration date: 11/17/2010

Table 1: Evidence Summary

Author, Year	Participants (n)	Study Design & Measures	Intervention	Findings/Conclusions
Lascalles, et al. 2010	40 cats (20 in each diet group)	10-week, blinded, parallel group, placebo controlled clinical study; owner-completed subjective surveys (activity-related behaviors); objective measures were captured using accelerometry	Cats were stratified based on high/low mobility impairment, then randomized to either a controlled-diet or degenerative joint disease-diet (green-lipped mussel extract and glucosamine/chondroitin sulfate) based on pain rating using a block design ; investigators were blinded.	<p>Evaluation of the owner's assessments revealed there were significant activity changes within groups and between groups, however, author acknowledges that type I error could have resulted.</p> <p>Objective measures revealed increased mobility for the test-diet ($P<0.001$) and a decreased in mobility for the controlled-diet ($P<0.001$)</p>
Aragon, et al. 2007	Systematic review of 16 studies	Examined a number of clinical trials that evaluated the efficacy of various joint disease treatments and of those, one study was reviewed that examined the efficacy of a mixture of chondroitin sulfate, glucosamine hydrochloride and manganese ascorbate	Quality rated a randomized, controlled trial (study design type I) involving 19 dogs that were given a combination of chondroitin sulfate, glucosamine hydrochloride and manganese ascorbate.	Results of the study indicated no improvement subjectively or objectively compared with dogs receiving placebo, and it was quality rated as insufficient for generalization.
McCarthy et, al. 2006	35 dogs	70-day randomized, double-blind, positive-controlled, multicenter clinical trial	Dogs were randomly assigned to two treatment groups: 1) Chondroitin sulfate/glucosamine hydrochloride (Synoquin® SA, Vet Plus Ltd.) or 2) Carprofen (Rimadyl®, Pfizer). Interval subjective assessments were conducted by veterinarians using a clinical scoring system.	Significant improvements ($P<0.001$) in pain, weight-bearing and overall condition scores were found at day 70 when compared to pre-treatment assessment scores
Neil, et al. 2005	n/a	Review article	Provide veterinary practitioners with information regarding the mechanism of action, pharmacokinetics, clinical efficacy, and safety of glucosamine and chondroitin sulfate	<p>When used in combination in vitro, results support the chondroprotective effect.</p> <p>Orally administered glucosamine and chondroitin sulfate are rapidly absorbed in dogs.</p> <p>For both glucosamine and chondroitin sulfate, safety profiles are good and seem to have few side effects, may be a good alternative to nonsteroidal anti-inflammatory drugs (NSAIDs).</p> <p>Beneficial effects of glucosamine and chondroitin sulfate, alone and in combination, have been established in vitro in several species.</p> <p>Determination of the minimal effective concentration of these compounds and beneficial effects in dogs and cats require further investigation.</p>


Table 1: Evidence Summary (cont'd)

Author, Year	Participants (n)	Study Design & Measures	Intervention	Findings/Conclusions
Adebowale, et al. 2001	8 Beagle dogs	Characterized the bioavailability and pharmacokinetics of chondroitin sulfate and glucosamine by performing a single dose bioavailability and dose proportionality study and a multiple dose pharmacokinetic study	<p>Study 1) Randomized three-way crossover study with a one-week washout period between treatments</p> <ul style="list-style-type: none"> Dogs randomly assigned to one of three treatments 1. IV solution of 500 mg glucosamine HCL and 400 mg of low molecular weight chondroitin sulfate 2. Product equivalent to 3 double strength Cosequin®/Cosamin® caps 3. Product equivalent to 4 double strength Cosequin®/Cosamin® caps Blood and plasma samples were analyzed <p>Study 2) Multiple dose open study</p> <ul style="list-style-type: none"> Dogs received a supplement equivalent to 3 double strength Cosequin®/Cosamin® caps from days 1 to 7 and then received a supplement equivalent to 6 double strength Cosequin®/Cosamin® caps from days 8 to 14 Blood and plasma samples were analyzed 	This study revealed that glucosamine and chondroitin sulfate are bioavailable after oral dosing and low molecular weight chondroitin sulfate results in significant accumulation upon multiple dosing.

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Call for authors: The Banfield Applied Research & Knowledge (BARK) team invites veterinary practitioners to author a critically appraised topic (CAT) for future issues of the Banfield Journal. If you are interested in contributing a CAT, please e-mail: BARK@banfield.net.

Ashlee Addleman, MPH, graduated from Portland State University in 2004 with a Bachelor of Science degree in Community Health Studies and received her Master of Public Health degree from Walden University in 2010. Her master's practicum and dissertation focused on research synthesis, population-based research, and evidence-based medicine and practice. Ashlee joined the Banfield Applied Research & Knowledge team as a research project specialist in 2006 and has been with Banfield, The Pet Hospital, since 2002. 

ATTACHMENT C

Clinical evaluation of a nutraceutical, carprofen and meloxicam for the treatment of dogs with osteoarthritis

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The efficacy, tolerance and ease of administration of a nutraceutical, carprofen or meloxicam were evaluated in a prospective, double-blind study on 71 dogs with osteoarthritis. The client-owned dogs were randomly assigned to one of the three treatments or to a placebo control group. The influence of osteoarthritis on the dogs' gait was described by comparing the ground reaction forces of the arthritic dogs and 10 normal dogs. Before the treatments began, and 30 and 60 days later, measurements were made of haematological and biochemical variables and of the ground reaction forces of the arthritic limb, and subjective assessments were made by the owners and by the orthopaedic surgeons. Changes in the ground reaction forces were specific to the arthritic joint, and were significantly improved by carprofen and meloxicam but not by the nutraceutical; the values returned to normal only with meloxicam. The orthopaedic surgeons assessed that there had been an improvement with carprofen and meloxicam, but the owners considered that there had been an improvement only with meloxicam. The blood and faecal analyses did not reveal any changes. The treatments were well tolerated, except for a case of hepatopathy in a dog treated with carprofen.

OSTEOARTHRITIS is a slowly progressive, degenerative and incapacitating disease, in which there is a reduction in the rate of synthesis of cartilage and an imbalance between the amounts of proteolytic enzymes and their inhibitors, mediated by proinflammatory cytokines (Dean and others 1989, Martel-Pelletier and others 1991, Dijkgraaf and others 1995). High levels of proinflammatory cytokines have been measured in synovial fluid from affected joints, although there is no sign of inflammation characterised by the infiltration of neutrophils and macrophages (Goldring 2000). The second isoform of the enzyme prostaglandin endoperoxide H synthase (PGHS) (PGHS-2 or cyclooxygenase-2) is inducible by proinflammatory cytokines and other mediators, implying that it contributes to inflammation and osteoarthritis (Amin and others 1997, Smith and others 2000). In dogs, developmental arthropathies such as elbow and hip dysplasia and some acquired arthropathies caused by articular fractures and ligament injuries (mainly rupture of the cranial cruciate ligament) can initiate this degenerative process (Martinez 1997, Martinez and Coronado 1997).

It has been established that the anti-inflammatory and undesirable side effects of the inhibitions of PGHS by the use of non-steroidal anti-inflammatory drugs (NSAIDs), were affecting two distinct isoforms of the enzyme, PGHS-1 and PGHS-2 (Vane and others 1998, Smith and others 2000). This discovery stimulated intense research to develop NSAIDs that would selectively, or preferentially, inhibit PGHS-2 and allow them to be administered daily without signs of toxicity (DeWitt 1999). A recent study reported a possible role of PGHS-1 in inflammation, and a protective and anti-inflammatory role for PGHS-2 (Gilroy and Colville-Nash 2000), reversing the previously assumed interaction between the PGHSs, inflammation and osteoarthritis. In addition, the inconsistency between the results of experimental studies of the selectivity of NSAIDs towards PGHSs, indicates that there is a need to evaluate the efficacy of these drugs and their potential for adverse effects (Ricketts and others 1998, Vane and others 1998, Kay-Mugford and others 2000).

To determine the most appropriate treatment, it is also necessary to consider the non-traditional agents, including many nutraceuticals, which have been proposed to reduce the clinical signs and prevent the degenerative process. A mixture of chondroitin sulphate, glucosamine hydrochloride and manganese ascorbate (CS-G-M) has previously been shown to provide prophylactic protection against synovitis (Canapp

and others 1999), to retard the degenerative process synergistically (Lippiello and others 2000) and to modulate the metabolism of articular cartilage (Johnson and others 2001). There have been controlled clinical trials of the efficacy of this mixture in the treatment of osteoarthritis in human beings (Leffler and others 1999, Das and Hammad 2000), but not, to the authors' knowledge, in dogs. Meloxicam, a preferential inhibitor of PGHS-2, has been shown to reduce the clinical signs of osteoarthritis in a subjective clinical assessment of dogs with the condition (Doig and others 2000) and in an objective analysis of the gait of dogs with synovitis induced chemically (Cross and others 1997). Meloxicam also has positive metabolic effects on human arthritic cartilage in vitro (Blot and others 2000). Improvement was also obtained with carprofen, an inhibitor of both isoforms of PGHS, in a subjective clinical assessment (Holtzinger and others 1992), in an objective analysis of gait (Vasseur and others 1995), and by reducing the early structural changes in a canine model of osteoarthritis (Pelletier and others 2000). In addition, in an in vitro experiment, carprofen stimulated the rate of synthesis of glycosaminoglycan (Benton and others 1997).

The aim of this clinical, prospective, randomised, double-blind study was to evaluate the efficacy, tolerance and ease of administration of these two NSAIDs and a nutraceutical product, in order to identify the best treatment for dogs with osteoarthritis. The results were evaluated in three ways: by a subjective evaluation by the owners, by a subjective clinical evaluation by a veterinary orthopaedic surgeon, and by an objective analysis of the gait of a group of dogs with chronic arthritic pathologies.

MATERIALS AND METHODS

Eligibility

To be included in the study the dogs had to weigh more than 20 kg and be more than 18 months old. They had to show radiographic evidence of osteoarthritis in one or two elbows, one or two stifles or one or two hips. The pathology had to be the cause of lameness (as determined by a complete orthopaedic examination) which was reported by the owner to be chronic and stable. Dogs with abnormalities of gait involving both fore- and hindlimbs were rejected, and only dogs with clinical signs of osteoarthritis of the elbows, hips or stifles were included. Dogs which had had a rupture of the

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TABLE 1: Scoring system* for the owners' subjective assessment of their dog's activity and signs of pain

Activity and sign of pain	Score
Activity	
Walking	
Getting up after a prolonged rest	
Running	
Climbing stairs	
Going down stairs	
Playing or exercising	
Jumping	
Assessment of ability to perform activity	
No difficulty in performing this activity	1
Slight and occasional difficulties in performing this activity	2
Frequent slight difficulty in performing this activity	3
Constant and obvious difficulty in performing this activity	4
Cannot perform this activity	5
I cannot evaluate this activity of my dog properly	x
Assessment of signs of pain and discomfort	
Shows no signs of discomfort or pain	1
Shows occasional signs of pain or discomfort, but with no link to a specific activity	2
Shows signs of pain or discomfort after exercise and/or rest periods	3
Shows signs of pain constantly	4

* Scores were added to produce a cumulative score. The same questionnaire was used at the second and third visits, except for the addition of these two questions: Was the administration of the medication really easy, not really easy or difficult? Did you notice any side effects linked with the use of this drug? None, lost appetite, vomiting, depression, diarrhoea, blood in stools, increased water intake or others

cranial cruciate ligament were admitted only if the rupture had been surgically repaired more than a year previously, or if it had been diagnosed more than a year previously, without surgical correction, and there was no evidence of instability (drawer movement) when they were examined. During the study, no concurrent treatment for osteoarthritis was allowed, and if a dog had previously received a treatment, the following withdrawal periods were observed: two weeks for oral NSAIDs, three weeks for oral corticosteroids, 12 weeks for injectable formulations, four weeks for oral nutraceuticals, and 24 weeks for injectable formulations of polysulphated glycosaminoglycans. Pregnant bitches, dogs which were reported to be hypersensitive to NSAIDs, dogs with a neurological or musculoskeletal pathology other than osteoarthritis, and dogs which had had orthopaedic surgery within the same year were excluded. Dogs were recruited through telephone calls, using the medical files of the veterinary teaching hospital of the Université de Montréal, and through advertisements in newspapers. The owners of dogs involved in the study were required to sign a consent form. A control group consisting of normal and breed-matched dogs, as determined by orthopaedic, neurological and radiographical examinations, was also included.

Study protocol

The experimental protocol was approved by the Animal Care and Use Committee of the Université de Montréal and was in accordance with the Guidelines of the Canadian Council for Animal Care. When the owners and their dogs arrived at the veterinary teaching hospital for the first visit, the owners were asked to complete a subjective owner assessment (Table 1). The dogs were weighed and their gait was analysed objectively by measuring ground reaction forces (GRFs) with a biomechanical force plate (Model OR6-6; Advanced Mechanical Technology). A visual examination of the dogs' gait and a complete orthopaedic examination were then made by one of two surgeons. If the disease affected both joints, only the most affected joint was evaluated. The orthopaedic surgeons were never aware of the GRF values, had no contact with the own-

TABLE 2: Scoring system* for the subjective orthopaedic assessment

Clinical parameter	Scoring system	Score
Lameness	Stands, walks and trots normally	0
	Stands normally, slight algetic gait when trotting	1
	Stands normally, slight algetic gait when walking	2
	Stands normally, evident algetic gait when walking	3
	Stands abnormally, evident algetic gait when walking	4
Articular mobility	No limitation of movement or crepitus	0
	10 to 20 per cent decrease in range of motion, no crepitus	1
	10 to 20 per cent decrease in range of motion with crepitus	2
	20 to 50 per cent decrease in range of motion	3
	More than 50 per cent decrease in range of motion	4
Articular pain	No sign of pain	0
	Mild pain (dog turns head in recognition)	1
	Moderate pain (dog pulls limb away or wants to move away)	2
	Severe pain (dog vocalises and becomes aggressive)	3

* Scores for the three clinical parameters were added to produce a cumulative score

ers and did not know which treatment was assigned. An orthopaedic score was attributed by the surgeon to the joint responsible for the clinical signs and lameness (Table 2); this score was called the subjective orthopaedic assessment. If there was uncertainty about which was the most affected joint, as determined by the orthopaedic examination and the objective GRF analysis, the objective criterion was used in making the decision. If both joints gave the same GRF values, the most severely arthritic joint, as shown on radiographs, was chosen. The elbows, hips and stifles of the dogs were radiographed while the dogs were sedated. Radiographs of other joints were taken if abnormalities were detected during the orthopaedic examination. A radiographic score for osteoarthritis was attributed to each joint (Table 3).

Blood samples were taken from each dog for the determination of the haematological variables: packed-cell volume, haemoglobin, red blood cell count, mean corpuscular haemoglobin concentration, mean corpuscular volume, white blood cell count, platelets, neutrophils, lymphocytes, monocytes, eosinophils, basophils, and a qualitative observation for toxic neutrophils, poikilocytosis and anisocytosis; in addition, the following biochemical variables were determined: glucose, urea, creatinine, alanine aminotransferase, alkaline phosphatase, total protein, albumin, globulin, albumin:globulin ratio, calcium, phosphorus, potassium, sodium, chloride, total carbon dioxide and anion gap, and faecal occult blood.

TABLE 3: Scoring system for the radiographic evidence of osteoarthritis

Articulation	Radiographic sign	Score
Hip	Osteophytes and sclerosis absent	0 (none)
	Acetabular remodelling, Morgan line, slight neck remodelling and slight femoral head sclerosis	1 (mild)
	Acetabular remodelling and osteophytosis, neck remodelling, enthesiophytosis, and femoral head sclerosis	2 (moderate)
	Advanced acetabular and neck remodelling, severe osteophytosis and advanced femoral head sclerosis	3 (severe)
	Osteophytes absent	0 (none)
Stifle	Osteophytes present on patella and proximal aspect of femoral trochlear groove	1 (mild)
	Osteophytes present on patella, femoral trochlear groove, medial and lateral femoral condyles and tibial plateau	2 (moderate)
	Severe osteophytes on patella, femoral trochlear groove, medial and lateral femoral condyles and tibial plateau; subchondral sclerosis of femoral condyles and tibial plateau	3 (severe)
	Osteophytes absent	0 (none)
Elbow	Osteophytes less than 2 mm on the anconeal process of ulna	1 (mild)
	Osteophytes 2 to 5 mm on the anconeal process of ulna, osteophytes on the head of radius less than 2 mm, and on the humeral crest less than 2 mm	2 (moderate)
	Osteophytes more than 5 mm on the anconeal process of ulna, osteophytes on the head of radius more than 2 mm, and on the humeral crest more than 2 mm	3 (severe)
	Osteophytes absent	0 (none)
	Osteophytes less than 2 mm on the anconeal process of ulna	1 (mild)

TABLE 4: Numbers of dogs with different joints affected by osteoarthritis which were treated with chondroitin sulphate, glucosamine hydrochloride and manganese ascorbate (CS-G-M), carprofen or meloxicam and evaluated by different methods

Treatment	0	Day 30	Day 60	Objective gait analysis	Subjective assessments	Blood and faecal analyses
CS-G-M						
Elbow	4	4	4	NA	NA	4
Hip	7	7	7	7	7	7
Stifle	8	8	8	6	7	8
Combined*	19	19	19	17	18	19
Carprofen						
Elbow	3	3	3	NA	NA	3
Hip	7	7	7	6	7	7
Stifle	7	6	6	5	5	6
Combined*	17	16	16	13	14	16
Meloxicam						
Elbow	4	4	4	NA	NA	4
Hip	6	6	6	6	6	6
Stifle	7	6	6	6	6	6
Combined	17	16	16	16	16	16
Placebo						
Elbow	4	4	NA	NA	NA	4
Hip	7	7	NA	7	7	7
Stifle	7	6	NA	6	6	6
Combined*	18	17	NA	17	17	17

NA Not applicable

* Includes elbows, hips and stifles

One of four treatments was assigned to each eligible dog by using a computer-generated random list. For treatment 1, dogs weighing between 20 and 45 kg received two capsules of CS-G-M (CosequinDS; Nutramax Laboratories) in the morning and one in the afternoon, orally for 30 days and then one capsule every 12 hours for the next 30 days. Dogs weighing over 45 kg received two capsules of CS-G-M every 12 hours for 30 days, and then two capsules in the morning and one in the afternoon for the next 30 days. Each capsule contained 500 mg of glucosamine hydrochloride, 400 mg of chondroitin sulphate and 75 mg of manganese ascorbate. For treatment 2, the dogs received 2.2 mg/kg carprofen (Rimadyl; Pfizer) orally, every 12 hours for 60 days. For treatment 3, the dogs received 0.2 mg/kg meloxicam (Metacam; Boehringer Ingelheim) orally on the first day and then 0.1 mg/kg orally, daily for 59 days. For treatment 4, the dogs received the same volume of meloxicam vehicle (placebo) as the dogs receiving treatment 3, for 30 days. The placebo was administered for only 30 days for ethical reasons.

On days 30 and 60, the owners brought their dogs back to the veterinary teaching hospital for a second and third visit. At these visits they were asked to complete a questionnaire, and they had been asked to bring back the unused product to verify that their dogs had received the treatments. The clinical evaluations made at the first visit were repeated, except for the radiographs.

Experimental procedure

The GRF values were measured with a biomechanical force plate, permanently mounted level with the floor and interfaced with a dedicated computer using software (Vetforce; Sharon Software) specially designed for the acquisition, storage and analysis of the data. The dogs were trotted over the force plate at between 1.9 and 2.2 m per second, by timing each passage with a chronometer and by controlling the stance time. Data from a minimum of five valid trials were obtained, and the validity of the trials was determined as described by Rumph and others (1993).

The vertical GRF values analysed for the affected limb were the peak, impulse, time to peak and time of the vertical GRF. The peak, impulse, and time to peak for the braking and propulsive portions of the craniocaudal GRF were also analysed. The forces (expressed as a percentage of bodyweight)

measured in the first five valid trials were averaged and the average was termed the gait profile of the arthritic limb. A gait profile was obtained before the treatment for the elbow, hip and stifle articulations. This profile contained the GRF values mentioned above for the evaluated limb and for both the fore- and hindlimbs. This same procedure was applied to the control group and was termed the non-arthritic gait profile. Blood samples were obtained by jugular puncture.

Dogs

Seventy-one dogs with clinical and radiographic evidence of osteoarthritis were used; in 15 of them the elbows were affected, in 27 the hips were affected and in the other 29 the stifles were affected. Fifty-eight of the dogs were pure breeds. They ranged in age from 18 to 144 months with a median of 68 months, and their median weight was 38 kg. Ten pure-breed dogs free of articular disease were used to obtain normal GRF values; they ranged in age from 29 to 93 months with a median of 45 months, and their median weight was 35 kg. Table 4 gives the numbers of dogs with osteoarthritis of the different joints which were allotted to the different treatments, and the numbers which were assessed objectively and subjectively.

Statistical analysis

To compare the dogs' response to the treatments, the Wilcoxon signed-rank test for paired data was used with a significance level of 1.7 per cent according to the Bonferroni adjustment for multiple comparisons. The gait profiles of the different articulations were compared by the Wilcoxon rank-sum test at a significance level of 5 per cent, to detect significant changes in the GRF values. The homogeneity between the experimental groups was evaluated with the Kruskal-Wallis one-way analysis of variance on ranks, and if necessary the Kruskal-Wallis Z test was used for testing multiple comparisons. Improvements were deduced when the GRF values changed towards the normal values, and when the owners' and orthopaedic surgeon's subjective scores decreased.

RESULTS

In 92 per cent of the cases, the owners reported that it was easy to administer the liquid suspensions (meloxicam and placebo) and the tablets or capsules (carprofen and CS-G-M). Table 4 shows the numbers of dogs from which samples of blood and faeces were analysed. The results of the post-treatment analyses provided no evidence of any abnormalities of clinical relevance. Four of the dogs had a positive faecal occult blood analysis at one re-evaluation; one was in the carprofen group and the others were in the CS-G-M group. The treatments were probably not involved because bones had been given to three of them and the diet of the other had been changed.

Three dogs did not complete the study. One 11-year-old Labrador retriever in the placebo group began to regurgitate food and developed dyspnoea and paresis shortly after the treatment started. It was diagnosed with a megaesophagus and later with myasthenia gravis. The owner opted for euthanasia before the second visit. A 10-year-old boxer in the meloxicam group began to vomit 10 days after the beginning of its treatment and its owner withdrew it from the study. A three-year-old Labrador retriever in the carprofen group became anorexic, lethargic and jaundiced and was vomiting. Its alanine aminotransferase activity was 31.4 times higher than the normal upper limit and its alkaline phosphatase activity was 4.4 times higher than the upper normal limit. The treatment was discontinued and it was diagnosed with toxic idiosyncratic hepatitis to carprofen; it was treated aggressively for 10 days and survived.

TABLE 5: Significant ($P<0.05$) decreases (-) and increases (+) in the ground reaction forces (GRFs) measured in osteoarthritic articulations in comparison with non-arthritic articulations

GRF value	Arthritic articulation		
	Elbow	Stifle	Hip
Forelimb			
Vertical			
Peak	-		
Impulse	-		
Time to peak	-		
Total time	-		
Craniocaudal			
Braking portion			
Peak	-	+	
Impulse	-	+	
Time to peak	-	-	
Propulsive portion			
Peak		+	
Impulse	-	+	
Time to peak	-		
Hindlimb			
Vertical			
Peak	+	-	-
Impulse	+	-	-
Time to peak	+		
Total time	+		
Craniocaudal			
Braking portion			
Peak	+	-	
Impulse	+	-	
Time to peak	+	-	-
Propulsive portion			
Peak	+	-	-
Impulse	+	-	
Time to peak	+		

At the beginning of the study the mean age, weight, affected limb GRF values, and the radiographic and subjective scores of the dogs in the four treatment groups were similar, and there was similarly no change in weight during the study that might have introduced a bias in the dogs' response to the treatments. Mediolateral GRF values were not investigated because of the wide variations reported by Rumph and others (1994) and DeCamp (1997).

Changes in GRF values

The GRF values of the dogs with osteoarthritis were compared with those of the control group of 10 breed-matched dogs with no evidence of osteoarthritis. Table 5 shows the significant changes in the direction of the GRF values in the dogs with osteoarthritis. There were 14 affected elbow articulations, 26 hips and 27 stifles. Two dogs were excluded because it was impossible to separate the vertical force-time curves of their fore- and hindlimbs. Two other dogs had evidence of tarsal and carpal pain at day 30 and were also excluded because they had radiographic evidence of mild osteoarthritis of a joint not included in the criteria.

Eight dogs were excluded from the objective gait analysis of the placebo group and three treatment groups; three failed to complete the study, one had an acute injury to a stifle joint without osteoarthritis and the other four were excluded for the reasons mentioned above. These dogs were also excluded from both subjective assessments.

The dogs which received a placebo for 30 days showed no significant response in terms of either the subjective assessments or the objective gait analyses. This result validated the comparisons of the treatment and placebo control groups.

Table 6 shows the significant effects on the GRF values of particular articulations of the dogs treated with carprofen and meloxicam, and the results of both subjective assessments. The results for the elbow articulation were not analysed because too few elbows were examined, but the combined subgroup was a combination of arthritic elbows, hips and stifles. Changes in GRF values common to the three articulations (Table 5) were further analysed as a combined subgroup. When there was a significant response in the GRF value specific to the hip or stifle subgroups, the value on day 60 (T_{60}) was compared with the normal GRF values, and if there was no significant difference the treatment was accepted as having restored the GRF value to normal.

The dogs treated with CS-G-M showed no significant response in terms of the objective gait analysis or either of the subjective assessments during the study.

There was a significant response in the results of the objective gait analysis of the dogs treated with carprofen, although the values did not return to normal. Compared with the baseline there was a response at day 60 in the vertical GRF peak

TABLE 6: Significant changes in the ground reaction forces (GRFs) of dogs with osteoarthritis after treatment with chondroitin sulphate, glucosamine hydrochloride and manganese ascorbate, carprofen or meloxicam, as determined by objective gait analysis and by subjective assessments. At day 60, the GRF values were compared with the mean GRF values of 10 normal dogs

Evaluation	Articulation subgroup	Treatment group	Response to treatment ($P<0.017$)	Normal GRF value ($P<0.05$)
Objective gait analysis				
Vertical GRF values				
Peak*	Combined†	Carprofen	$T_0 = T_{30} = T_{60} > T_0$	-
	Combined	Meloxicam	$T_0 = T_{30} < T_{60} > T_0$	-
	Hip	Carprofen	$T_0 = T_{30} = T_{60} > T_0$	No
	Stifle	Meloxicam	$T_0 = T_{30} < T_{60} = T_0$	No
Impulse*	Hip	Carprofen	$T_0 < T_{30} = T_{60} > T_0$	No
	Stifle	Meloxicam	$T_0 = T_{30} = T_{60} > T_0$	No
Craniocaudal GRF values				
Braking portion				
Peak	Stifle	Meloxicam	$T_0 < T_{30} = T_{60} > T_0$	Yes‡
Impulse	Stifle	Meloxicam	$T_0 < T_{30} = T_{60} > T_0$	Yes‡
Subjective orthopaedic assessment				
Orthopaedic score	Combined	Carprofen	$T_0 > T_{30} = T_{60} = T_0$	-
	Combined	Meloxicam	$T_0 > T_{30} = T_{60} = T_0$	-
Subjective owners' assessment				
Owners' score	Stifle	Meloxicam	$T_0 > T_{30} = T_{60} = T_0$	-

* GRF values commonly altered for the elbow, hip and stifle

† Includes elbows, hips and stifles

‡ Insignificant difference from the GRF values of 10 normal dogs

T_0 , T_{30} and T_{60} GRF values at day 0 (pretreatment), day 30 and day 60, respectively, - Applicable only to GRF values specific to the hip or stifle, = No significant improvement, < or > Significant improvement. In the subjective assessments an improvement was a decrease in scores and in the objective gait analysis an improvement was a positive modulation

value ranging from -3.39 to 17.02 per cent bodyweight, with a median value of 2.43 per cent. There was also a significant response at day 30 in the subjective orthopaedic assessment, the difference from baseline ranging from -5 to 1 with a median of -1. For the hip subgroup, a response was detected at day 60 for the vertical GRF peak and at days 30 and 60 for the vertical GRF impulse. There was no significant response in the owners' subjective assessment during the study.

In the group treated with meloxicam there was a significant response in the objective gait analysis, including a return to normal craniocaudal GRF values (braking portion) in the stifle subgroup. For the combined subgroup, the difference in GRF values at day 60 compared with the baseline ranged from -4.89 to 92.2 per cent bodyweight, with a median of 4.67. For the stifle subgroup, there was a response at day 60 for the vertical GRF peak and impulse. As with carprofen, a significant response was detected at day 30 in the subjective orthopaedic assessment of the combined subgroup, with the difference in orthopaedic score relative to baseline ranging from -6 to 1 with a median of -1. A significant response was detected at day 30 in the owners' subjective assessment of the stifle subgroup.

DISCUSSION

Kinetic gait analysis with a force plate provides a non-invasive, objective and quantitative evaluation of the forces between the foot and the ground during the stance phase of the stride (GRF). Analyses of GRF values have been widely used to evaluate surgical procedures (Dupuis and others 1994), to assess the effects of drugs (Budsberg and others 1999), and to investigate gait variations between breeds (Bertram and others 2000).

In this group of dogs with chronic arthritic articulations, the method demonstrated that osteoarthritis affected their gait and produced detectable changes in the GRF values of the arthritic and ipsilateral limbs. In the dogs with arthritic stifles, the forelimbs showed some positive changes in craniocaudal GRF values, and the hindlimbs showed some negative changes. As shown in Table 5, these changes were uncommon in dogs with arthritic hips when they were evaluated at the same velocity. The difference between the orthogonal forces patterns may be related to the aetiopathogenesis of arthritic stifles, possibly to a more pronounced inflammatory process, resulting in more severe lameness at the trot in these dogs. In the dogs with arthritic elbows, the positive changes in the hindlimbs may be related to the greater forces applied to the forelimbs and their effects on locomotion (Budsberg and others 1987).

Prostaglandins sensitise sensory neurons and reduce their activation threshold, thus enhancing their response to other stimuli (Dray 1995). One type of prostaglandin defined by its pentane ring substituents enhances the apoptosis of chondrocytes induced by an endogenous modulator (Notoya and others 2000). In one comparative *in vitro* study, carprofen and meloxicam were both shown to inhibit the synthesis of prostaglandin (PGE_2) (Ricketts and others 1998). NSAIDs must pass through the cell's lipid bilayer and reach the active site of the enzyme PGHS. They then compete directly with arachidonic acid for the active site and inhibit the biochemical process leading to the synthesis of precursors of prostaglandin (Vane and others 1998, Smith and others 2000, Thuresson and others 2001). From a structural chemical point of view, meloxicam (an enolic acid derivative) contains a side extension that could be responsible for its preferential inhibition of PGHS-2, either through a binding pocket specific to PGHS-2 or by exploiting a greater degree of flexibility at the apex of the enzyme (Hawkey 1999). This binding pocket is created by the structural difference between the two isoforms, three amino

acid substitutions creating the binding pocket and providing a wide access to the enzyme's active sites (Luong and others 1996, Smith and others 2000). Carprofen (a propionic acid derivative) contains a free carboxylic acid radical which is also present in aspirin and ketoprofen (Mancini and others 1995). This radical may inhibit the synthesis of prostaglandin precursors by blocking an active site of PGHS that is essential for high-affinity binding to arachidonic acid (Thuresson and others 2001).

In this study, these two NSAIDs with different molecular structures and one nutraceutical (CS-G-M) were evaluated for the symptomatic treatment of dogs with osteoarthritis, by comparing them with a placebo control. The fact that there was no change in the control group in terms of either the objective or subjective assessments of their gait validates this comparison and reinforces the results.

In terms of the owners' subjective assessment, no significant improvements were provided by either CS-G-M or carprofen over the 60 days of treatment. The recommended therapeutic dose of CS-G-M may have been insufficient to provide a clinical improvement, and larger doses or modifications to the proportions of its constituents may help to make it more effective, possibly in dogs with less severe osteoarthritis. The results obtained with carprofen were not in agreement with previous studies using the owners' subjective assessments (Holtzinger and others 1992, Vasseur and others 1995). However, the dogs treated with meloxicam improved significantly in terms of their owners' subjective assessment; it appeared to alleviate the dogs' arthritic lameness and allow them to resume normal daily activities.

The subjective orthopaedic assessments suggested that there were improvements with both NSAIDs; 30 days of treatment was sufficient to improve the dogs' mobility and reduce the signs of articular pain.

The similarity of the scores assigned at baseline and after 60 days by the subjective orthopaedic and owners' assessments was unexpected. NSAIDs inhibit the synthesis of precursors of prostaglandin, but some mediators involved in the degenerative process induce the synthesis of these precursors. For both NSAIDs the return to the pretreatment state, after some improvement, may be related to the presence of mediators responsible for enzymatic induction, pain and degenerative process, even when the synthesis of precursors of prostaglandin was inhibited. These arguments are based on clinical results and are thus limited in scope.

On the basis of the objective gait analysis, both NSAIDs improved the GRF values of the dogs with osteoarthritis, and improved their gait. However, only meloxicam restored some of the GRF values to normal. The craniocaudal GRF values give some information on the dogs' deceleration and acceleration, as indicated by the braking and propulsive fractions of this force. When treated with meloxicam, the dogs with arthritic stifles were able to decrease their momentum during the trot in a normal manner. If arthritic stifles implied a major inflammatory process and/or some immunological factors related to the aetiopathogenesis of osteoarthritis, PGHS-2 could be up regulated. As a result, treatment with meloxicam could improve articulations with a more severe inflammatory process. Higher peak vertical GRF values (common to elbows, hips and stifles) were observed after 60 days of meloxicam treatment.

There were no significant changes in the biochemical or haematological results in any of the treated dogs. Similar results have been reported in other studies (McKellar and others 1994, McNamara and others 1996, Forsyth and others 1998). However, one abnormal reaction was observed in one of five Labrador retrievers which were treated with carprofen. A final diagnosis of toxic hepatitis to carprofen was based on the similarity of the dog's clinical signs and biochemical results to earlier descriptions (McPhail and others

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1998). In this retrospective study, 61.9 per cent of the cases that showed toxic idiosyncratic hepatitis with carprofen were labrador retrievers (McPhail and others 1998).

In this study of a relatively small number of dogs with moderate to severe osteoarthritis, meloxicam was found to be an appropriate treatment, especially for an arthritic stifle, in terms of its efficacy in improving the dogs' gait and ability to live a more normal life, and the absence of side effects.

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Persistent truncus arteriosus and patent foramen ovale in a Simmentaler x Braunvieh calf

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A Simmentaler x Braunvieh calf had been anorexic during its first 36 hours of life, had a loud heart murmur and was suspected to have pneumonia. In the light of the results of radiographic and echocardiographic examinations, right heart catheterisation and angiography, a diagnosis of persistent truncus arteriosus and patent foramen ovale was made. The diagnosis was confirmed on postmortem examination.

PERSISTENT truncus arteriosus is a rare but serious cardiac malformation in human beings and domestic animals (Boon 1998, Friedman and Silverman 2001, Mair and others 2001). It is defined as a congenital cardiovascular malformation in which one great vessel, guarded by a single semilunar valve, forms the outlet of both ventricles and gives rise to the systemic, pulmonary and coronary arteries; it is associated with a ventricular septal defect (Crupi and others 1977, Butto and others 1986, Friedman and Silverman 2001). Persistent truncus arteriosus results from a failure of septation of the embryonic truncus by the infundibular truncal ridges (Crupi and others 1977, Friedman and Silverman 2001, Mair and others 2001).

Persistent truncus arteriosus has been diagnosed post-mortem in calves (Zschokke 1900, Kemler and Martin 1972, Heath and Kukreti 1979, Sandusky and Smith 1981, West 1988, Camon and others 1995, Reppas and others 1998), horses (Rooney and Franks 1964, Daniels 1974, Greene and others 1975, Rang and Hurtienne 1976), cats (Buergelt and Suter 1968, van de Linde-Sipman and others 1973), dogs (Chen and others 1972, van Mierop and others 1978), piglets (van de Linde-Sipman and Wensing 1972), and a lamb (Milstein and others 1982). To the authors' knowledge, the condition has been diagnosed antemortem only in horses (Sojka 1987, Steyn and others 1989, Tschudi and others 1997, Stephen and Abbott 2000).

This paper describes the results of a clinical examination, radiography, echocardiography, right heart catheterisation, angiography and postmortem examination of a calf with persistent truncus arteriosus communis and patent foramen ovale.

CASE REPORT

History

A six-day-old Simmentaler x Braunvieh calf had been anorexic during the first 36 hours after birth, had a loud heart murmur and was suspected to have pneumonia.

Physical examination

The calf was quiet and responsive. Its body condition was poor. Its rectal temperature was 39.4°C and its peripheral body temperature was markedly low. The mucous membranes were pale and the capillary refill time was two seconds. Its jugular veins were distended and a venous pulse was detectable. The heart rate was 160 beats per minute, and the heart beats were strong and regular. A loud radiating pansystolic heart murmur was audible on both sides of the thorax (grade 5/6 on the left side with a precordial thrill, and grade 4/6 on the right side). The calf's respiratory rate was 60 breaths per minute with an abnormal abdominal effort. Auscultation of the thorax revealed abnormally loud inspiratory and expiratory lung sounds.

Arterial blood gas analysis

A blood sample was collected from the right femoral artery, with the calf in right lateral recumbency, and analysed within five minutes of collection with an ABL 500 Radiometer (Radiometer GmbH). The results showed that the calf had marked hypoxaemia (pO₂ 60.9 mmHg, sO₂ 86.2 per cent) and evidence of a mild metabolic acidosis (pH 7.33, bicarbonate 17.2 mmol/litre, base excess -7.2 mmol/litre, pCO₂ 34.5 mmHg).

Thoracic radiography

Thoracic radiographs, taken in lateral and ventrodorsal projections, revealed moderate to severe cardiomegaly with dilatation of the left atrium and right heart enlargement (Fig 1). The lungs showed a generalised increase in interstitial radio-opacity and a distinct vascular pattern indicating pulmonary hyperperfusion and probable interstitial pulmonary oedema.

Echocardiography

Echocardiographic examinations were made with the calf standing (ATL Ultramark 9; Advanced Technology Laboratories)

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Clinical evaluation of a nutraceutical, carprofen and meloxicam for the treatment of dogs with osteoarthritis

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ATTACHMENT D

Efficacy of an oral nutraceutical for the treatment of canine osteoarthritis

A double-blind, randomized, placebo-controlled prospective clinical trial

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Keywords

Dogs, osteoarthritis, glucosamine, activity monitor, chondroitin

Summary

Objectives: To assess the safety and efficacy of an orally administered nutraceutical (Glu/CS+; + for additional ingredient) for the treatment of clinical osteoarthritis (OA) in dogs.

Methods: In this double-blind, randomized, placebo-controlled clinical trial, client-owned dogs with clinical signs of OA in one or more joints were assigned to a Glu/CS+ (n = 30) or placebo (n = 30) group. Dogs were administered Glu/CS+ or placebo orally and wore an activity monitor (AM) continuously throughout a 97 day study period. Prior to the initiation of the treatment, seven days of baseline activity was collected. On days -7, 30, 60 and 90 of the study, owners completed a pa-

tient assessment form (Canine Brief Pain Inventory). Data between groups were compared.

Results: No serious adverse events were reported. No difference was found between groups when evaluating daily activity counts during the seven-day pre-treatment period and the 90-day treatment period. Owner assessment (pain interference and pain severity scores) improved over the 90-day treatment period for both groups, however no difference was found between treatment groups.

Conclusions: Treatment with oral Glu/CS+ for a 90 day treatment period when compared to placebo treatment did not result in a significant increase in activity counts in dogs with clinical OA. However, owner assessment scores similarly improved throughout the study period for dogs in both groups, suggesting a caregiver placebo effect in this outcome measure.

osteoarthritis is to provide relief of inflammatory pain, and therefore improve quality of life (4). Conventional therapies such as non-steroidal anti-inflammatory drugs (NSAID) are commonly used in dogs with osteoarthritis, and the clinical benefits derived from this treatment are well recognized (4–5). However, NSAID can be associated with undesirable side effects such as kidney and liver toxicity as well as gastrointestinal ulceration or perforations (5–6). In an attempt to explore the use of alternative therapies, nutritional supplements, such as glucosamine hydrochloride (Glu) and sodium chondroitin sulfate (CS) are often integrated into multimodal treatment plans for dogs with osteoarthritis (7–9). Clinical trials in dogs using subjective or objective outcome measures evaluating combinations of Glu/CS are limited and reveal variable clinical efficacy (10–13). In addition, systematic reviews examining the use of nutraceuticals in dogs with osteoarthritis reached the conclusion that the evidence of the efficacy of nutraceuticals is poor, with the exception of diets supplemented with omega-3 fatty acids, and further studies with more objective measurements of outcome are needed (14, 15).

One study using only subjective assessments of outcome compared a Glu/CS combination to a positive control, carprofen, in dogs with chronic lameness, stiffness, joint pain and radiographic evidence of hip and elbow osteoarthritis for a 70 day treatment period (10). Dogs within the carprofen arm of treatment showed significant improvements from the baseline in all five parameters during the treatment

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Introduction

Osteoarthritis is a slowly progressive degenerative condition that most frequently involves the tissues of the synovial joints

and is characterized by pain and lameness associated with pathological changes within the joints and loss of articular cartilage (1–3). A primary goal for the treatment of the clinical signs observed in dogs with

period. Dogs receiving the Glu/CS showed statistically significant improvements from the baseline, specifically in regards to pain, weight-bearing and overall condition scores at 70 days. In contrast, a randomized, double-blind placebo-controlled study in client-owned dogs with chronic osteoarthritis in one or two elbows, stifles or hips assessed the efficacy of treatment with Glu/CS (with addition of manganese), carprofen, meloxicam or placebo (11). This study used ground reaction forces and subjective clinical assessments by an orthopaedic veterinary surgeon and owners. Statistically significant improvements in the ground reaction forces and subjective orthopaedic surgeon assessments were found in dogs receiving meloxicam and carprofen, but dogs receiving the placebo or the Glu/CS and manganese product showed no statistically significant improvements in any of the outcome measures. In addition, a more recent prospective, randomized, double-blinded trial in client-owned dogs with osteoarthritis evaluated the therapeutic efficacy, tolerability and safety of type-II collagen alone, in combination with Glu/CS or placebo using both subjective and objective outcome measurements (12). The Glu/CS treatment group had a significant reduction in pain on subjective assessments, however the ground reaction forces remained unchanged.

In human literature, clinical efficacy of these supplements is often drawn into question. A network meta-analysis reviewing the effects of Glu/CS or their combination or placebo in human patients with osteoarthritis of the hip or knee resulted in an assessment of 10 trials comparing the reduction of joint pain and radiographic evidence of joint space narrowing (16). The analysis concluded that Glu/CS did not reduce joint pain nor did it have an impact on joint space narrowing and suggested that health authorities and insurers not cover the costs of these treatments. Furthermore, a Cochrane database systemic review evaluated the benefits and safety of chondroitin for treating osteoarthritis compared with placebo or a comparator oral medication (not limited to NSAID, analgesics, opioids, and glucosamine) (17). Forty-three randomized controlled trials were evaluated and these trials, mostly of

low quality, revealed chondroitin was better than placebo in improving pain associated with osteoarthritis. Although the benefit was small and some of the differences persisted, they recommended that more high-quality studies are needed to assess the benefits of chondroitin in osteoarthritis, and the popularity of chondroitin as an over-the-counter supplement could be related to its associated low risk. Efficacy of clinical interventions in the veterinary profession largely rely on the veterinarian and owner assessments for determination of outcomes (18, 19). While these assessments are important, measuring objective changes in the patient after an intervention would complement conclusions about the efficacy of the treatment. Interest has grown in the use of activity monitors (AM) as an objective outcome measurement in dogs with osteoarthritis to assess the efficacy of treatment interventions within a dog's day-to-day environment (20–22). Activity monitors have been shown to detect a treatment response in dogs with osteoarthritis in a randomized, placebo controlled trial evaluating an NSAID (20). The AM used in that study contained an accelerometer which continuously measured the occurrence and intensity of motion for set periods of time which are stored in the form of activity counts (AC); this allows for AC to be documented before and after an intervention.

Because of conflicting reports regarding the benefits of Glu/CS in veterinary patients and the variety of ingredients included in nutraceutical products, the objective of this study was to determine the safety and efficacy of a commercially available Glu/CS^a product compared to placebo treatment in dogs with clinical signs of osteoarthritis in one or more joints over a 90 day treatment period. Our null hypothesis was that treatment group would not influence daily owner questionnaire scores or patient activity counts.

^a Dasuquin: glucosamine hydrochloride, sodium chondroitin sulfate and avocado/soybean unsaponifiables power: Nutramax Laboratories, Inc., Edgewood, MD, USA

Materials and methods

The Institutional Animal Care and Use Committee at the College of Veterinary Medicine at the University of Minnesota approved this study. All clients received a detailed description of the protocol and signed and informed consent form prior to the screening process. Inclusion criteria were as follows: dogs had to be nine months of age or older, weigh 5 kg or more, have a medical history and physical examination findings (performed by a single ACVS Diplomate or single ACVS surgical resident) consistent with chronic osteoarthritis (greater than three months duration) in one or multiple joints, and have confirmed radiographic evidence of osteoarthritis on orthogonal radiographs in the affected joint(s) (See also ► Appendix Tables 1 and 2: Available online at www.vcot-online.com). Dogs had to be in good health (based on veterinary examination) and have no clinically significant abnormalities on a pre-enrolment complete blood count and serum biochemistry. Complete blood counts and serum biochemistry were repeated at the conclusion of the study period. Dogs had to be removed from glucocorticoids, opioids, nutraceuticals, joint specific diets, or any over-the-counter supplements for four weeks and NSAID administration for two weeks prior to enrolment. Dogs that had received intra-articular injections (e.g. hyaluronic acid, polysulfated glycosaminoglycan, corticosteroids, stem cells, platelet rich plasma or other) within three months preceding or had joint surgery performed within six months prior to enrolment were not included. In addition, clients with planned changes to their dog's routine/day-to-day activities, such as a vacation or moving, throughout the study period were excluded. An Excel based random group generator^b was used prior to the study initiation for randomization of groups and was facilitated by a technician who was not involved in patient assessments. Dogs were enrolled in the study and placed in their group in order of the predetermined ran-

^b Excel: Microsoft Corporation, Redmond, WA, USA

domization. Owners and all staff involved in any clinical observations, assessments, or data analysis were blinded to treatment group assignment. Medication was first dispensed to owners on day 0 after completion of baseline data collection. Two technical staff were designated for dispensing and instructing clients how to administer the treatments. All treatments were removed from their original packaging and concealed in bags with labelled instructions for administration. Dogs in the placebo group were dosed with a single soft chew, chicken flavoured dog treat^c once daily for 90 days that did not contain any anti-inflammatory ingredients. Dogs in the Glu/CS+ group were dosed by weight per labelled instructions according to manufacturer, and because of this, some dogs received more than one soft chew treatment during the study, but all dogs in this group were still only dosed once daily.

Clients completed a Canine Brief Pain Inventory (CBPI; <http://www.vet.upenn.edu/research/clinical-trials/vcic/penn-chart/cbpi-tool>) questionnaire addressing the dog's osteoarthritis pain and function prior to enrolment (Day -7) and at each follow-up visit thereafter (days 30 \pm 3, 60 \pm 3 and 90 \pm 3). Day -7 served as the baseline score for the CBPI (23). Questions 1–4 in the CBPI were summed to establish pain severity score (PSS) and questions 5–10 were summed to establish a pain inference score (PIS); only dogs with a PSS and PIS \geq 2 were enrolled (23–24). Activity counts were measured with an AM^d device attached to a collar^e worn on the dog's neck (20–22, 25). Collars were individually fitted to each dog and a specific hole on the collar used was marked to allow consistency with tightness in placement throughout the study period. Owners were instructed not to place a leash or use any lead attachment to the device collar (26–27). The AM was placed on dogs at the end of the day -7 hospital visit and on follow-up visits (days

0 \pm 1, 30 \pm 3, 60 \pm 3 and 90 \pm 3) the battery in the collar was replaced and the AM data was downloaded, this process was minimized to less than 10 minutes. The days between day -7 to day 0 served to establish a baseline value for each patient so that changes in the patient's AC after the administration of an intervention could be assessed. The AM is waterproof and clients were instructed that the device should not be removed for bathing or swimming, a leash should not be attached to the AM collar and their dog should wear the collar continuously throughout the duration of the trial. The accelerometer-based AM continuously records the occurrence and intensity of motion. The AM stored the information in the form of AC and was set for one-minute epoch lengths. On day 0, data from the AM was downloaded and treatments were dispensed and clients were counselled on the administration of the test articles by a dispenser.

A physical examination was performed at each scheduled or unscheduled visit. A rescue protocol was in place if a dog's clinical signs or symptoms of osteoarthritis worsened and additional interventions (NSAID and/or analgesics) were medically indicated. Pet owners incurred no costs for participation and were compensated with a six-month supply of the test nutraceutical upon completion of the study.

Statistical analysis

All data until the dog completed the study or was rescued from the study were included in the analysis. The accelerometer data are continuous, repeated measures data with multiple pre-treatment (baseline) measurements and covariates. Total daily activity count reported by the AM was statistically evaluated. After the initial data analysis step of verifying distributions, calculating summary statistics and data checking, the change in the groups over time and individual daily differences were compared using a repeated-measures analysis of variance. Baseline days (days -7 to 0), group assignment (Glu/CS+ or placebo), CBPI scores, and the baseline day to group interaction were assessed as independent variables; post-intervention days

(days 0 to 90) were assessed as the dependent variables. Time, group, and the time to group interaction were assessed. To test for a difference in rescue rates between the two treatments, a logistic regression on rescue with treatment as the predictor was used. A p-value of <0.05 was considered statistically significant.

Results

Study population

Sixty (n = 30/group) clinically healthy client-owned dogs were enrolled in the study from a single institution. No statistical difference was found between groups for sex distribution, mean body weight distribution (Glu/CS+ 26.3 \pm 11.3 kg and placebo 27.7 \pm 11.2 kg) and mean age of dogs (Glu/CS+ 8.5 \pm 3.1 years and placebo 7.8 \pm 2.8 years). A total of 13 dogs were withdrawn from the clinical study for treatment failure – six of 30 in the Glu/CS+ group and seven of 30 in the placebo group as no difference in treatment failure rate was identified.

Adverse events

No serious adverse events were found. Within the Glu/CS+ group, one dog had a single episode of vomiting, and within the placebo group one dog experienced a single episode of vomiting and two had an episode of diarrhoea. These adverse events resolved without the addition of veterinary care. One dog in the placebo group developed a urinary tract infection and was treated with antibiotic medication during the study period. All dogs enrolled in the trial (including treatment failure cases) had repeat complete blood count and serum biochemical analyses after completion of the study and no clinically significant changes were noted.

Treatments

According to client reports and monthly review of the treatments dispensed, all dogs received the prescribed treatment for days 0 through 90. The CBPI pain severity questions 1–4 and pain interference questions 5–10 significantly decreased over time

c Hill's Science Diet Canine Soft and Chewy Training Treats: Hill's Pet Nutrition, Inc., Topeka, KS, USA

d Actical Respironics Mini Mitter: Philips Respironics, Bend, OR, USA

e ¾ inch Collar Strap: SportDOG, Knoxville, TN, USA

from day -7 for both groups (► Figure 1, ► Figure 2). There was no difference between groups at any time point for either CBPI pain severity questions 1–4 or pain inference questions 5–10. There was no difference between groups at any time point.

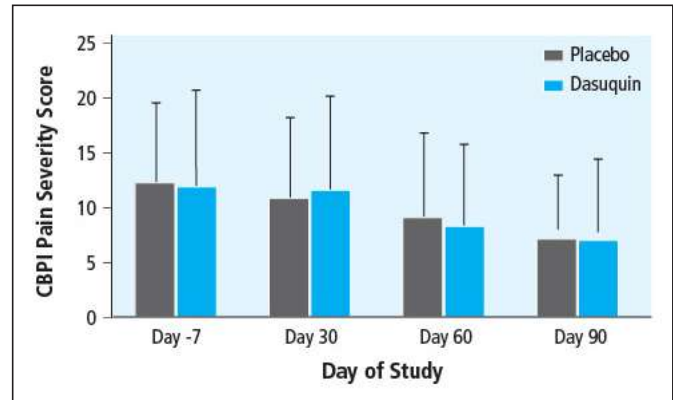
Mean daily AC remained statistically similar over the baseline and treatment periods regardless of group ($p = 0.91$ for placebo treated group; $p = 0.83$ for Glu/CS+ treated group). When mean daily AC for each individual day after intervention were compared, a single statistical difference was identified. On day 3 after treatment, AC were significantly increased ($p = 0.03$) in dogs treated with Glu/CS+. No significant differences were found between groups in the remaining 89 of 90 treatment days and mean daily AC were greater numerically in the placebo group in 52 of the 90 (57.8%) treatment days (► Figure 3).

Discussion

In this randomized, placebo-controlled, clinical trial we found treatment group did not influence daily owner questionnaire scores, treatment failure rate, or patient activity counts; thus, we failed to reject our null hypothesis. There are conflicting reports regarding the potential therapeutic benefits of Glu/CS products in veterinary medicine (10–13). For example, there is evidence that various glucosamine/chondroitin products are bioavailable in the dog and provide a treatment benefit in induced canine models of osteoarthritis (28–31). Contributions to therapeutic variation include differences in study design and additives in Glu/CS product studied. These differences make it difficult to draw an all-encompassing conclusion regarding Glu/CS products safety and efficacy in dogs. Given these mixed findings, we elected to design a clinical trial that tested the safety and efficacy of a Glu/CS+ product as the sole treatment for osteoarthritis in dogs. The results of this study do not support a therapeutic effect from Glu/CS+ in dogs with spontaneous osteoarthritis, but we cannot comment on its overall efficacy given the limited number of dogs ($n = 30$) and duration of treatment (90 days). For

Figure 1

The sum \pm SD of Canine Brief Pain Inventory (CBPI) questions 1–4 evaluating pain severity. A significant decrease over time was found in both the placebo treatment (black) and Glu/CS+ treatment (blue) groups. No difference between groups was found.



comparison, a treatment response has been reported using this AM in dogs with osteoarthritis; one study ($n = 35$) reported an increase in total activity counts in dogs treated with carprofen and another study ($n = 13$) reported an increase in total activity counts in dogs treated with canine-specific anti-nerve growth factor antibody (20, 32). The potential benefits of Glu/CS in dogs with osteoarthritis has been questioned not only due to the limited scientific clinical evidence, but also the lack of information on variation in absorption, pharmacokinetics, and the mechanism of action remains largely unknown.

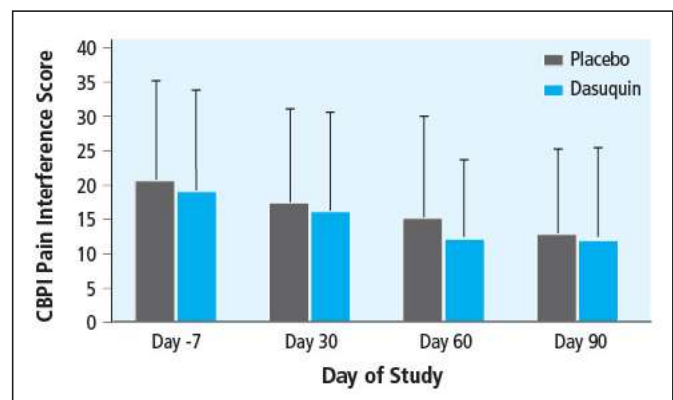
In this study, a similar proportion of dogs (6/30 Glu/CS+; 7/30 placebo) were withdrawn from the study because of treatment failure. This can serve as an alternative method to look at the efficacy of a treatment; again there was no difference between groups. The treatment failure rate was higher than reported in some studies where no dogs (treatment or placebo

treated) were rescued (20, 32). A reasonable explanation for this is the duration of the study. The duration of this study was longer and all but three dogs were rescued in the first four weeks of treatment (► Appendix Tables 1 and 2: Available online at www.vcot-online.com).

This study used both subjective and objective outcome measures. Recently it has been recommended that until a consensus has been reached regarding the outcome measures used to assess canine osteoarthritis, an inclusion of at least one existing, validated outcome measure in each future study is needed (18–19). Since this study investigated the systemic treatment effect of an oral intervention in dogs with osteoarthritis, often in multiple joints, we elected to focus on outcome measures that report on the patient in its natural environment. We also wanted to balance subjective evaluation of the patient with objective changes in the patient. We elected not to use force platform gait analysis as many of

Figure 2

The sum \pm SD of Canine Brief Pain Inventory (CBPI) questions 5–10 evaluating pain inference. A significant decrease over time was found in both the placebo treatment (black) and Glu/CS+ treatment (blue) groups. No difference between groups was found.



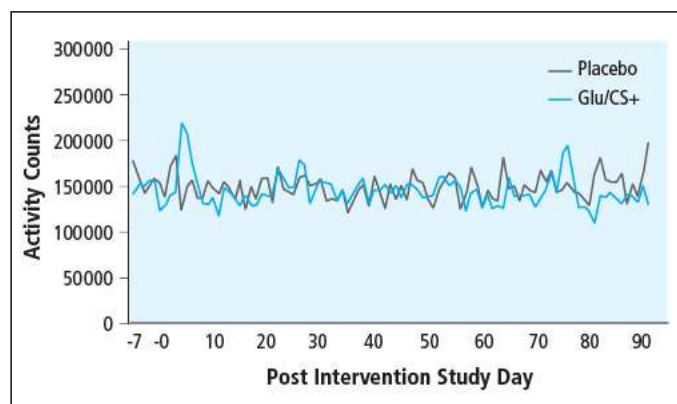


Figure 3
Mean daily activity counts over the treatment period in the placebo treatment (black line) and Glu/CS+ treatment (blue line) groups. Glu/CS+ was significantly greater on Day 3; no other differences were found.

the dogs enrolled in this study had multiple joints affected by osteoarthritis, thus limiting the utility of force platform gait analysis as an outcome measure. For efficacy, we used the CBPI and an AM that have been previously validated as outcome measures in patient populations with similar characteristics to those in this study (20–25). We used owner reporting of adverse events, veterinary physical exams and patient blood work to evaluate safety.

The owner subjective assessment used within this study (CBPI) has been previously validated in dogs with osteoarthritis and owner information is useful for the assessment of the dog outside of a hospital setting. The previously described caregiver placebo effect was found to be common in the evaluation of a patient response to treatment not only within the pet owners, but also veterinarians (33). In this study, placebo treated dogs had significantly improved CBPI pain severity and pain interference scores. At the same time, activity counts (objective outcome measure) for dogs in the placebo treated group remained unchanged over time. This supports a conclusion that there was a caregiver placebo effect associated with the owners of the dogs in this study population.

Ideal statistical analysis of activity monitor data remains open for debate. We compared total daily activity counts between groups on a daily basis, change over the entire study period between groups, and the frequency of which group had numerically greater activity counts. This is similar to previous studies looking for a treatment effect in dogs with osteoarthritis (20, 32). We did not report activity intensity even

though it has been previously reported in dogs that the AM that was used in this study could be used to distinguish between sedentary, walking, and trotting activities (34). We elected to not investigate this outcome measure because activity intensity in a previous study was addressed in 15 second epochs over a three minute period, and in this study dogs were studied for three months (34). We are not suggesting that activity intensity is not important, only that it remains challenging to investigate it over an extended period of time. It is also important to note that while we used the term “validated” with respect to AM, we remain unsure how to translate the clinical relevance of these data with respect to the distance travelled by the pet wearing the AM.

To the authors’ knowledge, the long-term safety of Glu/CS and related nutritional supplement products in dogs has not been reported. Adverse reactions reported in veterinary literature primarily involved gastrointestinal signs (10–11). In the present study, one adverse event was reported within the Glu/CS+ group (vomiting) and three within the placebo group (1 vomiting; 2 diarrhoea), all of which resolved without veterinary intervention. In addition, there were no significant changes in the pre-screening biochemical or haematological results as compared to the 90 day repeat in any of the dogs. Although Glu/CS+ proved to be safe in this study population, we cannot comment on its overall safety given the limited number of dogs ($n = 30$) and duration of treatment (90 days). There are several potential study biases that could have influenced the outcome of this

study. We did not block randomize based on patient signalment (e.g. body weight, body condition score, age, gender, breed, duration of disease). Duration of disease certainly could be a study bias. In this study, overall mean patient age exceeded eight years and duration of disease had to be greater than three months for inclusion in the study. We found determining exact duration of disease difficult since most of our patients were older patients with osteoarthritis secondary to hip or elbow dysplasia, and with clinical signs that began when the patient was younger and had continued for several years. It is well known that patient size influences reporting from activity monitors. We elected to control these potential biases via randomization, blinding and including a placebo treatment group. Additionally, we evaluated these biases by statistically testing for the presence of group differences - none were found. We also did not randomize based on characterization of the osteoarthritis (e.g. location(s), aetiology, severity, duration). Intuitively, not all osteoarthritis is the same. For example, bilateral hip osteoarthritis secondary to hip dysplasia with a six year duration may respond differently to an intervention than unilateral elbow osteoarthritis secondary to osteochondrosis with a three month duration. We did not address these potential concerns in this study because, in practice, the product studied is used for nearly all types of osteoarthritis.

In this randomized, placebo-controlled, clinical trial we found Glu/CS+ did not have a beneficial treatment effect when compared to placebo treatment when evaluated by daily owner questionnaire scores and patient activity counts

Author Contributions

RS and MC were responsible for the conception and design of the study. All authors were all involved in the data acquisition, analysis and interpretation, and all authors were involved in the drafting or revising of the manuscript and approved of the submitted version.

Conflict of interest

There are no conflicts of interest to declare.

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ATTACHMENT E

BURSOR FISHER

P.A.

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SUITE 940
WALNUT CREEK, CA 94596
www.bursor.com

L. TIMOTHY FISHER
Tel: 925.300.4455
Fax: 925.407.2700
ltfisher@bursor.com

July 11, 2022

Via Certified Mail - Return Receipt Requested

Compana Pet Brands
707 Spirit 40 Park Drive
Suite 150
Chesterfield, MO 63005-1137

Re: *Notice And Demand Letter Pursuant To California's Consumers Legal Remedies Act, Cal. Civ. Code § 1750, et seq.; U.C.C. §§ 2-313, 2-314, 2-607; and all other relevant state and local laws*

To Whom It May Concern:

This letter serves as a preliminary notice and demand for corrective action by Compana Pet Brands ("You") on behalf of our client, Linda Goshert, and a class of all similarly situated purchasers of Doggie Dailies-branded glucosamine supplements (the "Supplements").¹ This letter also serves as notice of claims arising from breaches of express and implied warranties described herein pursuant to U.C.C. §§ 2-313, 2-314, 2-607, as well as violations of consumer protection laws, including but not limited to California's Consumers Legal Remedies Act, Cal. Civ. Code § 1750, *et seq.*; California's Unfair Competition Law ("UCL"), Cal. Bus. & Prof. Code §§ 17200, *et seq.*, California's False Advertising Law ("FAL"), Cal. Bus. & Prof. Code §§ 17500, *et seq.*, and all other applicable federal and state laws.

You advertise the Supplements as products that help maintain and improve joint health. Specifically, the labels of the Supplements represent: "Promotes Healthy Joints, Comfort, and Mobility." You continue these representations online such as on Amazon's webpage, where Ms. Goshert made her purchase: "Doggie Dailies is a safe and effective hip and joint soft chew your dog will love. Our glucosamine dog treats are specially formulated to help promote healthy joints, mobility, and flexibility. A daily dose of Doggie Dailies soft chews can help support your dog's mobility and overall joint health."

However, decades of studies² and peer-reviewed tests have repeatedly shown that supplements containing glucosamine and chondroitin (the active ingredients in the Supplements)

¹ The Supplements include Doggie Dailies Advanced Hip & Joint Supplement for Dogs, Doggie Dailies Senior Essentials Advanced Hip & Joint, and Doggie Dailies Senior Essentials 10-in-1 Senior Multivitamin.

² The studies include: Moreau, M., et al., *Clinical Evaluation Of A Nutraceutical, Carprofen And Meloxicam For The Treatment Of Dogs With Osteoarthritis*, Vet. Record No. 152 at 323-29 (2003); Scott, et al., *Efficacy Of An Oral Nutraceutical For The Treatment Of Canine Arthritis: A Double-Blind Randomized, Placebo-Controlled Prospective Clinical Trial*, Vet. Comp. Ortho. Traumatol., 30 at 318-23 (2017).

do not improve joint function in dogs or reduce pain, leaving consumer paying a fortune for a hocus pocus that never materializes. Nonetheless, You prey on consumers who are willing to do anything to relieve their dog's pain with the full knowledge that what consumers are purchasing is worthless. Accordingly, Your representations are false and misleading and constitute unfair methods of competition and unlawful, unfair, and fraudulent acts or practices, undertaken by You with the intent to result in the sale of the Products to the consuming public. Your representations also constitute breaches of the express and implied warranties.

Ms. Goshert, is, and at all times, has been a citizen of California, residing in Fort Bragg, California. Ms. Goshert has purchased Doggie Dailies Advanced Hip & Joint Supplement for Dogs on multiple occasions from Amazon.com, including as recently as approximately March 2022. In doing so, Ms. Goshert saw the false and misleading claims that the Supplements contributes to joint health and reduces joint pain. Ms. Goshert understood these claims to be representations and warranties that the Supplements would lead to joint health and reduce joint pain. Ms. Goshert reasonably relied on these representations and warranties in deciding to purchase the Supplements, and these representations were part of the basis of the bargain in that she would not have purchased the Supplements, or would not have purchased them on the same terms, if true facts had been known. As a direct result of Your material misrepresentations and omissions, Ms. Goshert suffered economic injuries.

Therefore, these acts and practices violated, and continue to violate, the CLRA in at least the following respects:

- a. in violation of 1770(a)(4), You have used deceptive representations with respect to the Supplements;
- b. in violation of 1770(a)(5), You have represented that the Supplements have characteristics and benefits they do not have;
- c. in violation of Section 1770(a)(7), You have represented that the Supplements are of a particular standard, quality, or grade, when they are not; and
- d. in violation of Section 1770(a)(9), You have advertised the Products with an intent not to sell them as advertised.

On behalf of Ms. Goshert and the Class, we hereby demand that You immediately: (1) cease and desist from engaging in the foregoing violations; and (2) make full restitution to all Class members of all purchase monies obtained from sales thereof.

We also demand that You preserve all documents and other evidence which refer or relate to any of the above-described practices including, but not limited to, the following:


1. All documents, communications, reports, and memoranda concerning the advertisement, marketing, labeling, and packaging of the Supplements:

- a. Documents and communications discussing what text and/or images should be featured;
 - b. Documents and communications concerning Your decision to include the misrepresentations at issue, including but not limited to the glucosamine claims at issue;
 - c. Documents and communications concerning Your decision to exclude any disclosure indicating that the Supplements do not in fact contribute to joint health or reduce joint pain; and
 - d. Documents and communications concerning any changes made to the advertisement, marketing, labeling, and/or packaging of the Supplements during the Class Period.
2. All documents concerning the sale of the Supplements:
 - a. The total net revenue generated from the sale of the Supplements during the Class Period;
 - b. The total number of people in the United States who purchased the Supplements during the Class Period;
 - c. The total number of people in California who purchased the Supplements during the Class Period; and
 - d. The average amount paid for the Supplements.
 3. All documents, communications, consumer surveys, or memoranda concerning any testing or other research done, whether by You or by a third party, regarding the ingredients in the Supplements;
 4. All communications with customers concerning complaints related to the Supplements, especially concerning glucosamine.
 5. All documents concerning the identity of those individuals who purchased the Supplements; and
 6. All documents and/or communications between You and any retailer or wholesaler relating to the Supplements.

If you contend that any statement in this letter is inaccurate in any respect, please provide us with your contentions and supporting documents immediately upon receipt of this letter.

Please contact me right away at 925-300-4455 or ltfisher@bursor.com if you wish to discuss an appropriate way to remedy this matter. If I do not hear from you promptly, I will take that as an indication that you are not interested in doing so and will proceed accordingly.

Very truly yours,

A handwritten signature in black ink, appearing to read "L. Timothy Fisher". The signature is written in a cursive, flowing style with a long horizontal stroke at the end.

L. Timothy Fisher

ATTACHMENT F



5-in-1
Multivitamin

- Targets 5 Key Areas of Your Dog's Health
- Provides Antioxidant Support + Nutritional Support for Joints, Skin & Coat, Digestion and The Immune System
- Great for Dogs of All Sizes and Breeds

**DELICIOUS PEANUT BUTTER FLAVORED
SOFT CHEWS**



NET CONTENTS 16 OZ (453 g) | APPROX. 225 (2 g) CHEWS

Dog Supplement
For Dogs 6 Months or Older



GUARANTEED ANALYSIS

PER 1 SOFT CHEW



225 SOFT CHEWS PER JAR

RECOMMENDED DAILY DOSAGE

EPA (Eicosapentaenoic Acid)	– 1.7 mg
DHA (Docosahexaenoic Acid)	– 2 mg
Vitamin A	– 3500 IU
Vitamin D3	– 230 IU
Vitamin E	– 7 IU
Thiamine (Vitamin B1)	– 2 mg
Riboflavin (Vitamin B2)	– 1.15 mg
Pantothenic Acid	– 1.38 mg
Niacin	– 17 mg
Pyridoxine (Vitamin B6)	– 1.36 mg
Folic Acid (Vitamin B9)	– 204 mcg
Biotin	– 19 mcg
Vitamin B12	– 5 mcg
Ascorbic Acid (Vitamin C)	– 38 mg
Fructooligosaccharide (FOS)	– 95 mg
Glucosamine	– 47,500 mg/kg (95 mg per soft chew)

Omega-3 Fatty Acids	– 44 mg
Omega-6 Fatty Acids	– 13 mg
Omega-9 Fatty Acids	– 18 mg
Total Microorganisms (Aspergillus Oryzae, Aspergillus Niger, Trichoderma Reesei)	– 80 mg
Alpha-Amylase (Aspergillus Oryzae)(a)	– 240 FCC DU
Protease (Aspergillus Oryzae) (b)	– 880 FCC HUT
Lipase (Aspergillus Niger) (c)	– 8.8 FCC LU
Cellulase(Trichoderma Reesei) (d)	– 3.6 FCC CU
Papain (Papaya) (e)	– 200 FCC PU
Bromelain (Pineapples-Stem) (e)	– 160 FCC PU
Hemicellulase (Trichoderma Reesei)	– 4 FCC CU (d)

UP TO 25 POUNDS	➔	1 CHEW	✓
26 – 50 POUNDS	➔	2 CHEWS	✓
51 – 75 POUNDS	➔	3 CHEWS	✓
76+ POUNDS	➔	4 CHEWS	✓

Calorie Content (Calculated, ME)
= 1,800 kcal/kg, 3.6 kcal/soft chew.

FULL LIST OF INGREDIENTS: Lecithin, Chickpea Flour, Peanut Flour, Pea Flour, Vitamin E Supplement, Niacin Supplement, d-Calcium Pantothenate, Riboflavin Supplement, Thiamine Mononitrate, Vitamin A Supplement, Pyridoxine Hydrochloride, Vitamin B12 Supplement, Folic Acid, Vitamin D3 Supplement, Biotin, Ground Flaxseed, Glucosamine HCl, Fructo-oligosaccharides, Dried Aspergillus oryzae fermentation extract, Dried Aspergillus niger fermentation extract, Dried Trichoderma reesei fermentation extract, Dried Pineapples-stem, Microcrystalline Cellulose Powder, Monoglycerides, Diglycerides, Glycerin, Honey, Ascorbic Acid, Dried Ground Carrot, Dried Ground Sweet Potato, Natural and Artificial Flavors, Cod Liver Oil, Salmon Oil, Sorbic Acid, Mixed Tocopherols (preservative), Rosemary Extract.